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MYXŒDEMA.[1]

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MYXŒDEMA is not a common disease, but it is by no means a rarity. The importance of its recognition lies in the fact that it is one of the diseases for which we have a specific remedy. Referring to the effect of treatment, the late William Osler said:

> The results, as a rule, are unparalleled by anything in the whole range of curative measures. Within six weeks, a poor, feeble-minded, toad-like caricature of humanity may be restored to mental and bodily health.

[1] Read at a meeting of the Section of Medicine of the New South Wales Branch of the British Medical Association on September 15, 1932.

Data.

During the last six years a study has been made of ten patients, suffering from myxœdema in its classical form, who were seen in hospital and private practice. Six patients with atypical or incomplete myxœdema have also been observed and treated. Reference is made to four patients suffering from ill-defined symptoms suggestive of hypothyreoidism, and to three patients with myxœdema, and to two cretins who were under treatment when they first came under observation.

In this paper it is proposed to discuss myxœdema, both typical and atypical, and to make frequent reference to the series of patients studied. Though small in number, they serve to illustrate many of the salient features of the disease.

Description.

Myxœdema may be described as being a chronic disease of insidious origin occurring commonly in

middle-aged persons, chiefly women. It is caused by a disorder of function of the thyreoid gland and is characterized by changes in the skin and subcutaneous tissues, loss of hair, mental hebetude and lowered metabolism.

Historical Note.

A brief reference to the history of the disease will not be out of place, for, as Professor George R. Murray has said, "the history of myxœdema, though short, is full of interest".

Attention was first drawn to the symptoms of the disease in 1873 by Gull, who called it "a cretinoid state supervening in adult life in women". Four years later W. M. Ord recorded the symptoms observed by himself in five cases, with *post mortem* appearances, including an advanced stage of atrophy of the thyreoid gland found in one of them by Professor W. S. Greenfield, and the result of the chemical examination of the skin by C. Charles. As Charles found an excess of mucin in the skin, Ord proposed the name myxœdema, by which the malady has since been known.

In 1882 J. L. Reverdin described a peculiar chain of symptoms which he had observed to follow total extirpation of the thyreoid gland for goître. In the following year, Kocher, of Berne, described this condition and named it *cachexia strumipriva*. The researches of Horsley and the investigation of the Committee of the Clinical Society of London, set on foot by Sir Felix Semon, made it clear that the changes following complete removal of the gland, *cachexia strumipriva*, myxœdema and sporadic cretinism were one and the same disease, due to insufficiency of the thyreoid gland.

The symptoms of the disease having thus been traced to the loss of the thyreoid gland, the next advance was in the direction of supplying the deficiency. Schiff and von Eiselberg showed that the transplantation of another thyreoid gland into the abdomen of an animal which had been submitted to thyreoidectomy averted the usual fatal result. Quite independently, in 1890, thyreoid grafting was suggested by Sir Victor Horsley as a method of arresting the disease in man. This suggestion was acted upon by several surgeons, especially by Bettencourt and Serrano, who noticed that in their case the operation was immediately followed by improvement; they attributed the improvement to absorption of the juice of the transplanted gland. Professor Murray regarded this observation as being of great importance, and concluded that it indicated that the thyreoid gland carried on its function by means of an internal secretion. He therefore suggested that the administration of an extract of the gland would remove the symptoms of myxœdema. In 1891 he commenced the treatment of a woman, aged forty-six years, suffering from myxœdema by means of hypodermic injections of the glycerin extract of the sheep's thyreoid gland. The symptoms rapidly disappeared, In 1892 it was shown by Howitz, of Copenhagen, and by Dr. Hector Mackenzie and Dr. E. L. Fox, of England, that the same results could be obtained by the simple method of giving thyreoid extract or the raw gland itself by mouth. Murray therefore continued treatment of his patient by means of the oral administration of thyreoid extract, and she lived to the age of seventy-four, when she died of heart disease.

Later, it was found that the administration of desiccated thyreoid gland would produce equally successful results.

Ætiology.

Alcoholism, syphilis, tuberculosis, acute infections such as erysipelas, typhoid fever, influenza, pneumonia and cholera, have all been mentioned by various authors as possible causes of myxœdema. But, except when the disease follows operative removal of the thyreoid gland or when the gland atrophies after the application of X rays, the ætiology is obscure. In none of the cases studied did any of these factors play a part. There are, however, certain factors which may be regarded as predisposing causes and are therefore worthy of consideration. These are: (i) sex, (ii) age, (iii) the previous occurrence of exophthalmic goître, (iv) family predisposition, and (v) climate.

Sex.—Myxœdema occurs much more frequently in women than in men. George Dock and H. Lisser state that women are more frequently affected than men in the proportion of seven to one. In Murray's series of 425 collected cases the proportion was approximately identical, 370 of the patients being women and only 55 men.

In the series of ten cases of classical myxœdema studied in this paper, there were nine women and only one man.

Multiparity may play some part in the predisposition to the disease. One patient had eleven, and a second ten children. Another patient, however, who had been married thirty-two years, was sterile.

Age.—George Dock and H. Lisser say that the average age of onset in women is thirty-eight years and in men forty-two years. Furthermore, they state that more than half the cases in women occur between the ages of forty and forty-five, and that the onset is frequently at the time of the menopause.

In the series under consideration the ages of the patients when they first came under observation were as follows: The youngest woman was 34, the eldest 66, and the average age was 50 years. The man was 50 years of age.

The Previous Occurrence of Exophthalmic Goître.—One natural mode of recovery from exophthalmic goître is by a gradual involution of the hypertrophied thyreoid gland accompanied by fibrosis. In some of these cases the beneficent process extends too far and results in atrophic fibrosis of the gland with myxœdema. One such case was found in the series studied. Her history is interesting.

She was first seen on June 25, 1931, and complained of nervousness, palpitation and diarrhœa of some months' duration. On examination it was noted that proptosis of the eyes, slight tremor of the hands, and very slight enlargement of the thyreoid gland were present. The pulse rate was 96 per minute. The basal metabolic rate was +17% and the blood serum cholesterol content was 134 milligrammes per hundred cubic centimetres (see

Figure I). In July, 1932, it was found that she was six months pregnant. Her facial appearance was changed and presented the typical picture of myxœdema. Supraclavicular pads were present. The basal metabolic rate had fallen

FIGURE I.

to −4% and the blood serum cholesterol had risen to 311 milligrammes per hundred cubic centimetres (see Figure II).

Family Predisposition.—There is apparently in some families a predisposition to thyreoidal disease, but it usually takes the form of predisposition to various forms of goître rather than to myxœdema.

Climate.—Myxœdema is seen mainly in white races living in temperate climates. It is said to be rare in coloured races. It is stated that the disease is more common in cold than in warm climates. In connexion with this it must be remembered, however, that since myxœdema is associated with a lowered metabolism, it would naturally make itself more obvious in a cold than a warm climate.

Other Factors.—Hans Curschmann[1] makes the interesting observation that "exogenous factors like overstress, worry and undernourishment, especially shortage of tryptophane, play an important part" in the causation of myxœdema. He states that during the war years, owing to the scarcity of such foods as meat, milk, eggs, cheese and wheat, which are rich in tryptophane, the number of cases of myxœdema rose tremendously, and that for the same reason the number of cases of Graves's disease fell sharply.

Pathology.

Apart from the changes in the thyreoid gland, consisting of interstitial fibrosis and atrophy of the acini, the most interesting and important lesions are found in the skin and subcutaneous tissues.

As previously stated, Charles considered that the thickness of the skin and subcutaneous tissues, the so-called "solid œdema", was due to an excess of mucin. The condition is now considered to be due partly to a tissue, resembling granulation tissue, containing an increased number of fibrils and nuclei and partly to an infiltration with an amorphous material resembling mucus in the lymph spaces. The cellular infiltration is most marked round the hair follicles, sebaceous glands and sweat glands.

It has been suggested that the tissue fluid in myxœdema is mostly intracellular and that the disturbance in the water metabolism is primarily due to changes in the permeability of the cell membranes.

An infiltration similar to that seen in the skin has been described as occurring in other organs.

Myocardial degeneration, arteriosclerosis and chronic nephritis are frequently associated with myxœdema and are considered by some authorities to be due to the disease, but as Nellis B. Foster points out, "with a malady which develops most frequently in the fourth, fifth and sixth decades of life, some caution is required in assigning to it a causal relation to cardiac, vascular and renal lesions which are also common at these same periods of life".

In view of the intimate relationship between the pituitary and the thyreoid glands, it is interesting to note that hyperplasia of the pituitary gland with increase of the colloid, involving especially the *pars intermedia*, has sometimes been noted at autopsy.

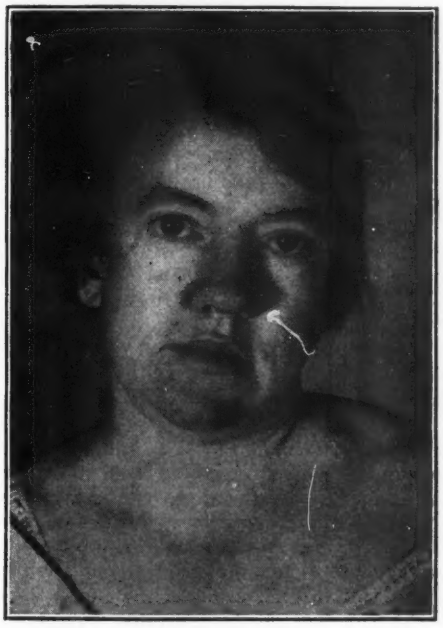

FIGURE II.

Clinical Features.

Although the clinical features of myxœdema are described in every text book of medicine, the disease

is not always recognized. As they are of paramount importance in the diagnosis of the malady, it will be valuable to review them.

Owing to the slow development of the morbid changes in the thyreoid gland and the consequent gradual failure of the glandular secretion, the onset of the first symptoms is often so insidious that it is frequently very difficult to ascertain their real duration. Speaking generally, most of the symptoms are referable to changes either in the mentality of the patient or in the skin and subcutaneous tissues.

Fatigue and malaise are frequent complaints. All the patients in this series complained of these symptoms. The mental processes are slow. It is said that many patients suffering from myxœdema are seen by psychiatrists on account of mental apathy. Frank psychoses are rare today, but were not uncommon prior to the advent of thyreoid medication. The speech is usually slow and the voice has been described as being "leathery". This feature was especially marked in the oldest patient of the series (see Figure III). On account of the alteration in voice, some patients with myxœdema have consulted laryngologists. Deafness sometimes occurs, and dimness of vision has been described as being associated with the disease. Neither of these features was noted in the series under discussion.

FIGURE III.

Owing to changes in the skin and subcutaneous tissues, undue sensitiveness to cold is usually a prominent feature of the disease. It was present in all the patients of the series. Failure of perspiration and loss of hair were the chief complaints of the only male member of the group (see Figures IV and V).

Constipation is almost invariably complained of by sufferers from myxœdema. Joint pains are often troublesome.

A somewhat rare symptom, menorrhagia, was present in one of the women patients (see Figures VI and VII).

The appearance of the patient is characteristic. The features are coarse and a "brutish" type of facies is present. The lips are thick and everted.

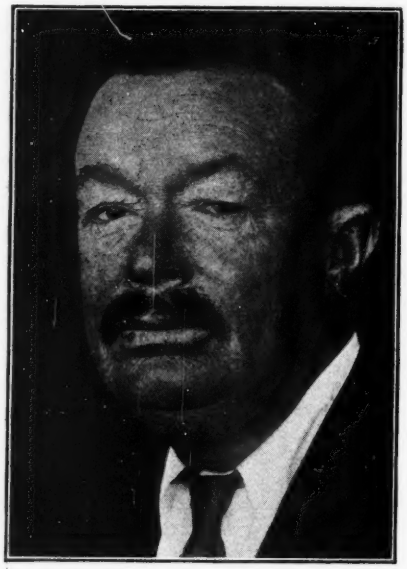

FIGURE IV.
Showing male patient after cessation of treatment for one year.

The eyelids are puffy and the forehead wrinkled. The skin is sallow or even yellow in colour. A malar

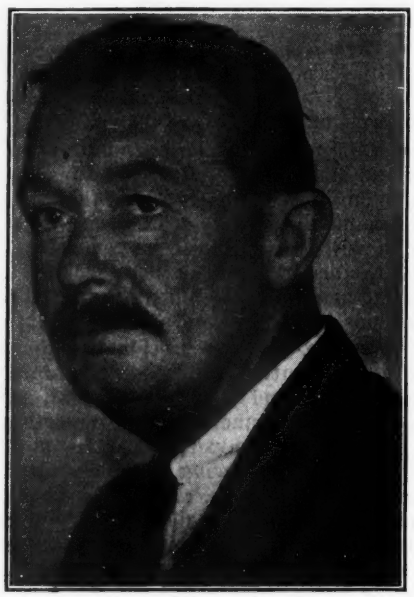

FIGURE V.
Showing patient seen in Figure IV three months after resumption of treatment.

flush is often present. The eyebrows are usually wasted, especially in their outer thirds. The hair becomes dry, coarse and brittle, and pulls out easily.

The edges of the hairy scalp are often affected, the resultant appearance being called the "frontal band alopecia" (D. Walsh) or the cassowary neck, according to the region affected (see Figure VIIIB). The axillary and pubic hair may be scanty or even absent. The skin is thickened, rough and scaly. The

FIGURE VI.
Showing patient before treatment.

shape of the hands has been described as spade-like —the "spade hand" (Gull). Soft gelatinous pads like fat appear in various parts of the body, but most frequently in the supraclavicular regions. The so-called "solid œdema" is a striking feature. No

FIGURE VII.
Showing patient seen in Figure VI, after two months' treatment.

pit is formed on pressure. Little or no isthmus of the thyreoid gland can be felt in front of the trachea.

Myxœdematous infiltration may involve the mucous membranes of the nose, mouth and pharynx. Difficulty and thickness in speech may be attributed in part to a swollen tongue.

The gait is of a waddling type and the muscles easily become fatigued. Ptosis of the viscera has been attributed to a relaxed abdominal wall.

The temperature is subnormal and the pulse is usually slow.

FIGURE VIIIA.
Showing patient in 1926, before onset of myxœdema.

FIGURE VIIIB.
Showing patient seen in Figure VIIIA in 1931.

Myocardial degeneration and arteriosclerosis are frequently found in patients suffering from myxœdema, but there is a division of opinion among

various authorities as to the causal relationship between the cardio-vascular degeneration and the disease.

In 1918 Zondek[2] described a dilatation of both the right and left sides of the heart associated with indolent heart action, which he believed to be peculiar to myxœdema, since the size of the heart decreased and its action improved following thyreoid medication.

Various abnormalities in the electrocardiogram have been described. Willius and Haines,[3] in a study of 162 cases of high grade myxœdema, found no cases of heart failure or organic cardio-vascular disease which could be justly attributed to myxœdema. Further, although Willius noted numerous electrocardiographic abnormalities, which disappeared under thyreoid medication, he was unable to satisfy himself of the existence of a cardiac syndrome characteristic of myxœdema. But Fahr[4] drew attention to the negative *T* waves in leads I and II, which he claimed became positive under thyreoid medication. In a few cases notched and widened *Q R S* complexes, due to delayed intraventricular conduction, disappeared under thyreoid medication.

There is a widespread belief that myxœdema causes arteriosclerosis. The majority of the cases of myxœdema present evidence during life (as shown in the retinal arteries), as well as *post mortem*, of arterial degeneration, but, as in the case of heart disease, it has not been demonstrated that this is cause and effect.

Furthermore, evidence of the relationship between arteriosclerosis and myxœdema is not lacking in the reports of necropsies in the older literature before thyreoid medication came into use, and from the experimental side the evidence is very suggestive that myxœdema induces arteriosclerosis.

The importance of the occurrence of arteriosclerosis and weakened cardiac muscle in association with myxœdema lies in relation to prognosis and treatment.

Attacks of *angina pectoris* have been reported after the commencement of thyreoid medication by C. C. Sturgis.[5]

It is interesting to note that Parsonnet and Hyman[6] have drawn attention to the occurrence of *angina pectoris* in diabetics suffering from myocardial lesions following the institution of treatment by insulin. Dr. L. W. Dunlop[7] last year referred to a patient suffering from *diabetes mellitus* complicated by arteriosclerosis, whom I treated in conjunction with him, and who suffered from attacks of heart block following insulin injections.

In two of the series studied the pulse pressures were very low. In one of these cases the systolic pressure was 90 and the diastolic pressure 80 millimetres of mercury, and the pulse pressure therefore was only 10 millimetres of mercury. Unfortunately, this patient was seen twice only and there was therefore little opportunity of observing her progress. In another case the radial arteries were palpable.

Secondary anæmia with leucopenia and slight lymphocytosis is sometimes present, but, although some degree of anæmia is characteristic of the disease, there is no constant blood picture. One peculiarity of the anæmia is its persistence after the more obvious signs of the myxœdema have disappeared. In one of the cases studied, facial pallor persisted for several months.

Owing to the accumulation of water, albumin and salt in the tissues, the plasma volume is decreased and the viscosity of the blood is increased. According to Deusch,[8] the total protein is increased from 5% to 9%.

George Dock and H. Lisser state that albuminuria occurs in one-fifth of the cases. None of the patients studied had albuminuria.

Glycosuria is uncommon, owing to the increased carbohydrate tolerance.

Atypical or Incomplete Myxœdema.

In discussing atypical or incomplete myxœdema we are on much less certain ground than in describing the clinical features of classical myxœdema.

According to F. M. Thurmon and W. O. Thompson,[9] "an underfunction of the thyroid is usually marked or else absent and a search for cases of hypothyroidism too mild to be myxœdematous is not as fruitful as one would anticipate". They were able to find only 13 such cases among 196 cases of lowered metabolism which they reviewed.

During the last decade, however, many mild types of myxœdema have been described. These are often difficult to differentiate from neurasthenia, psychasthenia and senility. Such symptoms as apathy, constipation, undue sensitiveness to cold, fatigue on slight exertion, pains in the joints, tingling in the extremities, menstrual irregularities and increasing weight, and the appearance of dryness of the skin and hair, slight thickening of the subcutaneous tissues and a malar flush may lead one to suspect the presence of hypothyreoidism and to apply the therapeutic test of the administration of thyreoid substance. Some degree of hypothyreoidism is frequently found at the menopause.

Although the administration of thyreoid extract benefits patients suffering from the so-called "hypothyreoidism without myxœdema", the results are far less dramatic than in the more defined cases of myxœdema. It is probable that in many cases the deficiency is pluriglandular, and one may venture the opinion that as therapeutically active preparations of the various glands of internal secretion are made available, the syndromes due to the absence of the various hormones will become more clearly differentiated.

Special Laboratory Investigations.

Two special laboratory investigations are of great value in confirming the diagnosis of myxœdema and in guiding the course of treatment.

These investigations are the determination of the basal metabolic rate and the estimation of the blood serum cholesterol content. The value of the former is well known, but the importance of the latter is not widely realized.

Basal Metabolic Rate.

It is a matter of common knowledge that the basal metabolic rate in myxœdema is invariably lower than the theoretical normal rate. There are, however, certain points which are worthy of discussion.

As mentioned in the discussion of atypical myxœdema, F. M. Thurmon and W. O. Thompson[9] investigated a series of 196 patients with lowered basal metabolic rates who were not suffering from myxœdema. The lowering of the metabolism varied from −11% to −45%. Of the 196 patients, 11 appeared to be healthy; 13 were considered to be suffering from a degree of hypothyreoidism too mild to be considered myxœdema—the patients in this group all showed striking clinical improvement after thyreoid medication; 172 suffered from a variety of symptoms and morbid conditions, including nervousness, worry, fatigue, scanty or absent menstruation, starvation, pituitary tumour and muscular atrophy.

Thurmon and Thompson stress the importance of muscle tone in the regulation of the basal metabolic rate, and consider that in the past there has been a tendency to attribute all low basal metabolism to an underfunction of the thyreoid gland. Further, they state that the mere association of a low basal metabolic rate with a disease is not evidence that the disease causes the low rate, as the metabolism may have been low before its onset. They conclude that, if the basal metabolic rate is below −25%, an underfunction of the thyreoid gland is probably present, but that if the depression of the metabolism is not greater than −21%, it cannot be assumed that the thyreoid function is impaired.

Rabinowitch,[10] in discussing "pitfalls in the clinical application and interpretation of the basal metabolic rate", also emphasizes the importance of the influence of muscle tone on the basal metabolic rate. He states that, according to prevalent views, muscular activity probably accounts for more than half of the basal metabolism. The low basal metabolic rates found in patients suffering from arthritis are, he says, not due to hypothyreoidism, but to the fixation of large masses of muscle round the damaged joints.

As Thurmon and Thompson also pointed out, Rabinowitch stresses the fact that certain individuals may have low basal metabolic rates and still be apparently normal. He states that: "the imperturbable, happy, overweight type who never gets flurried . . . may have a basal metabolism of − 15 to 20 per cent. and still be normal".

He considers that the tendency of the basal metabolism to be low after removal or destruction of the ovaries suggests that age and inactivity are not the only factors in the causation of a lowered basal metabolic rate at the menopause, and adds that patients with a lowered basal metabolic rate at this age do not, as a rule, respond very well to thyreoid therapy.

In the series of cases of classical myxœdema under consideration in this paper, the basal metabolic rates varied from −45% to −4% in the case of the woman who developed myxœdema subsequent to exophthalmic goître. A rate of −4% is certainly not a low rate for a patient suffering from myxœdema, but it must be remembered that she was six months pregnant at the time of the estimation and that the rate was previously +17%.

The man who had undergone treatment for three and a half years and had then ceased taking thyreoid substance for one year, had a basal metabolic rate of −11%. The basal metabolic rates of the other members of the series on whom the estimation was made were as follows: −16%, −22%, −26% and −31%.

In view of Rabinovitch's explanation of the lowered basal metabolic rates found in arthritis, it is interesting to note that a patient suffering from polyarthritis, who showed no improvement with thyreoid medication, had a basal metabolic rate of −20% (see Case 2, Table IIB).

Among other conditions in which low basal metabolic rates are found, may be mentioned lipoid nephrosis, certain cases of xanthomatosis, *diabetes mellitus*, hypopituitarism, Addison's disease and inanition.

Blood Serum Cholesterol Content.

Epstein and Lande,[11] in 1922, drew attention to the high blood cholesterol values found in myxœdema, and noted their decrease after the administration of thyreoid extract. They stated that:

> Once established in connection with the basal metabolic rate we believe that repeated cholesterol determinations offer a satisfactory method of following the course of thyroid toxicity. This is of special value in judging the effect of thyroid therapy in myxedema and allied conditions of hypothyroidism.

Elwyn,[12] in discussing the hypercholesterolæmia of lipoid nephrosis, suggests that as a result of the disturbance of colloidal combination of protein with fats and cholesterol esters in the border regions of the endothelial cells of the capillaries, some of the cholesterol in the cell is not properly retained and is taken up by the blood.

In view of this hypothesis it is of interest to note that in the discussion of the pathology of the "solid œdema" found in myxœdema reference was made to the suggestion that the disturbance in the water metabolism was primarily due to changes in the permeability of the cell membranes.

High blood cholesterol values have been observed also in nephritis with œdema, biliary obstruction, lipoid nephrosis, certain cases of xanthomatosis, and in *diabetes mellitus*. The readings are usually above the accepted average limits (160 to 200 milligrammes per 100 cubic centimetres) at the time of the menopause and in the later months of pregnancy.

In the series of ten cases of classical myxœdema the blood serum cholesterol estimations have proved valuable both from the point of view of diagnosis and of following the progress of treatment.

The highest reading was 1,000 milligrammes per 100 cubic centimetres and the lowest reading (the patient with myxœdema following exophthalmic goître) 311 milligrammes per 100 cubic centimetres.

With the exception of that case, the lowest initial reading in the series before the commencement of thyreoid therapy was 516 milligrammes per 100 cubic centimetres. With the institution of treatment the cholesterol values fell to figures approximating to the upper limit of normality (230 milligrammes per 100 cubic centimetres) or lower. In connexion with the patient with a blood serum cholesterol content of 311 milligrammes per 100 cubic centimetres, it may be argued that the occurrence of pregnancy would account for some of the increase in the cholesterol value.

In a series of six cases classified as incomplete myxœdema the blood serum cholesterol values were considerably lower, the highest reading being 400 and the lowest 210 milligrammes per 100 cubic centimetres. In these patients (see Figures IX, X, XI) many of the clinical features of myxœdema were present and all showed improvement in some respect after thyreoid therapy. The basal metabolic rate of the patient with a blood serum cholesterol content of 400 milligrammes per 100 cubic centimetres was −36% (see Figure XI).

FIGURE IX.

Estimations of the blood serum cholesterol content were also made in a series of four patients who presented one or two signs and symptoms suggestive of hypothyreoidism.

In this series the results were practically within normal limits, the highest reading being 246 in a patient at the menopause, and the lowest 160 milligrammes per 100 cubic centimetres in the patient previously mentioned as suffering from polyarthritis, whose basal metabolic rate was −20%.

In a series of five patients who were receiving thyreoid therapy when they first came under observation, the readings were within normal limits, varying from 220 to 170 milligrammes per 100 cubic centimetres.

The results of the estimations of the basal metabolic rate and of the blood serum cholesterol

FIGURE X.

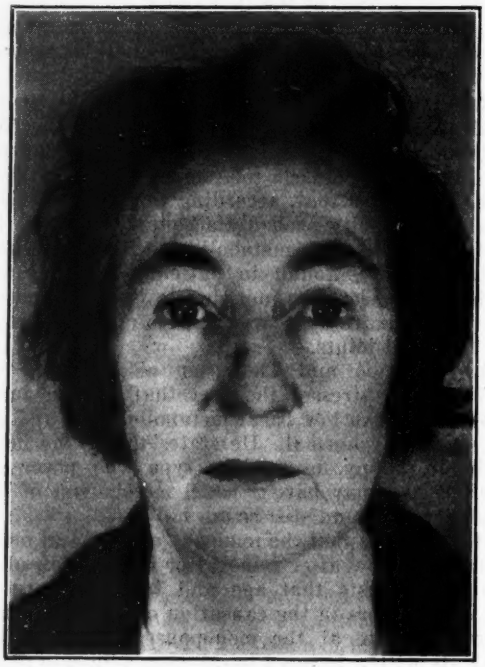

FIGURE XI.

content, together with various clinical observations in the different case groups, are shown in tabular form. In Table I the cases are all examples of classical myxœdema. In Table IIA cases of incom-

TABLE I.

Classical Myxœdema.

Case Number.	Date of First Consultation.	Sex.	Age.	Basal Metabolic Rate.	Blood Serum Cholesterol Content. Milligrammes per 100 cubic centimetres.	Remarks.
1	October 25, 1926.	Male.	50	— March 8, 1931. −11%	— March 8, 1931. 1,000 March 31, 1932. 246	Treated at hospital for five months. Lost one and a half stone in weight. Treated himself for three years. Reported again on March 8, 1931, after having no treatment for one year. (See Figures IV and V.)
2	February 3, 1927.	Female.	58	—	August 22, 1928. 173 April 27, 1932. 146	Clinical condition normal when the cholesterol estimations were made.
3	October 13, 1927.	Female.	38	October 28, 1927. −22%	August 12, 1928. 254	Clinical condition normal when the cholesterol estimation was made.
4	April 19, 1928.	Female.	63	—	April 26, 1928. 604 July 17, 1928. 250	
5	April 4, 1929.	Female.	47	April 9, 1929. −45% June 6, 1929. −23% October 10, 1929. −13% July 26, 1930. −21% October 5, 1930. −21% August 27, 1932. −23%	April 9, 1929. 571 May 9, 1929. 307 June 6, 1929. 252 August 15, 1929. 291 December 21, 1929. 339 July 26, 1930. 291 October 5, 1930. 291 February 19, 1931. 219 August 6, 1932. 232	Menorrhagia. (See Figure VI.) (See Figure VII.) Menstruating.
6	May 2, 1929.	Female.	37	−26%	613	Blood pressure: systolic 90, diastolic 80 millimetres of mercury. (Only attended hospital twice.)
7	May 16, 1929.	Female.	66	−31%	711	Advanced case; eleven children. Very little improvement after three months' treatment. (See Figure III.)
8	August 13, 1929.	Female.	52	—	516	Married 32 years; no children. Died on February 1, 1930.
9	June 25, 1931.	Female.	34	June 27, 1931. +17% July 7, 1932. −4%	June 27, 1931. 134 July 7, 1932. 311	June 25, 1931. Hyperthyreoidism symptoms: Nervousness, diarrhœa, palpitation. Signs: Proptosis, tremor, slight enlargement of thyreoid gland, pulse rate 96. (See Figure I.) July 7, 1932. Myxœdema: Dry skin and hair. Supraclavicular pads. Monotonous voice. Six months pregnant. (See Figure II.)
10	October 29, 1931.	Female.	54	November 5, 1931. −16%	November 5, 1931. 640 March 10, 1932. 234	Ten children. Persistent facial pallor. (See Figure VIII.)

plete myxœdema are shown. In Table IIB patients with ill-defined symptoms and signs suggestive of hypothyreoidism are shown. In Table III the patients were all under treatment when first seen, and presented no gross signs of thyreoid deficiency when the cholesterol estimations were made.

It is interesting to note that the combination of a lowered basal metabolic rate and a high blood cholesterol value is found in myxœdema, in lipoid nephrosis, in certain cases of xanthomatosis, and in *diabetes mellitus*, and that the first three of these conditions are benefited by thyreoid therapy.

TABLE IIA.
Incomplete Myxœdema.

Case Number.	Date of First Consultation.	Sex.	Age.	Basal Metabolic Rate.	Blood Serum Cholesterol Content. Milligrammes per 100 cubic centimetres.	Remarks.
1	October 18, 1928.	Female.	57	October 25, 1928. −6%	November 20, 1928. 278	General fatigue, constipation, dry skin, slight enlargement of thyreoid gland, pulse rate 64 per minute.
2	April 15, 1929.	Female.	54	April 29, 1929. −18%	March 9, 1929. 238	Rheumatoid arthritis, wasting of outer thirds of eyebrows, dry skin, hair falling out. Sensitive to cold. Blood pressure: systolic 176, diastolic 100 millimetres of mercury.
3	June 20, 1929.	Female.	31	August 26, 1929. −7%	June 26, 1929. 270	Sensitive to cold, dry skin, pulse rate 80 per minute, swelling on dorsum of right hand.
4	March 30, 1931.	Female.	50	August 30, 1932. −9%	August 25, 1932. 210	Dry skin, frontal band alopecia, outer thirds of eyebrows wasted. (See Figure IX.)
5	May 5, 1932.	Female.	48	June 9, 1932. −15%	March 12, 1932. 210	Increasing obesity. Slight puffiness of face. (See Figure X.)
6	July 25, 1932.	Female.	48	July 30, 1932. −36%	August 6, 1932. 400	Breathlessness, two years' duration; menopause one and a half years ago; hair dry, wasting of outer thirds of eyebrows; frontal band alopecia; blood pressure: systolic 206, diastolic 110 millimetres of mercury. (See Figure XI.)

TABLE IIB.
Ill-Defined Symptoms Suggestive of Hypothyreoidism.

Case Number.	Date of First Consultation.	Sex.	Age	Basal Metabolic Rate.	Blood Serum Cholesterol Content. Milligrammes per 100 cubic centimetres.	Remarks.
1	March 9, 1928.	Male.	43	—	219	Increasing obesity, dry skin.
2	November 23, 1928.	Female.	30	January 3, 1929. −20%	January 3, 1929. 160	Polyarthritis, dry skin.
3	December 2, 1929.	Female.	22	—	202	Dry scaly skin, asthma.
4	July 28, 1932.	Female.	44	—	246	Menses irregular, hot flushes, constipation.

TABLE III.
Treated Cases.

Case Number.	Date of First Consultation.	Sex.	Age.	Basal Metabolic Rate.	Blood Serum Cholesterol Content. Milligrammes per 100 cubic centimetres.	Remarks.
1	August 31, 1928.	Female.	43	—	August 31, 1928. 220	Myxœdema, treated six years.
2	March 4, 1929.	Male.	28	March 4, 1929. −20%	March 4, 1929. 183	Cretin, treated twenty years.
3	October 3, 1930.	Female.	50	November 23, 1929. −31%	July 7, 1931. 170	Myxœdema, treatment commenced on November 24, 1929.
4	November 8, 1930.	Female.	13	—	November 8, 1930. 202	Cretin, treated since twelve months of age.
5	March 24, 1932.	Female.	46	—	March 24, 1932. 188	Myxœdema, treated ten years.

Association with Other Diseases.

The association of myxœdema with cardiovascular changes has already been discussed.

It is not generally recognized that a severe anæmia may be the only conspicuous manifestation of myxœdema. Such cases have been reported by Mackenzie.[13] The blood counts resembled those found in pernicious anæmia, with the exception that alteration in the size and form of the red cells was slight. The patients responded rapidly to thyreoid therapy.

Weinstein[14] has recently reported details of two cases in which the combination of *diabetes mellitus* and myxœdema was found.

Langdon Brown[15] mentions that one of the first patients with myxœdema treated in England by means of thyreoid extract developed *diabetes mellitus* after thirty years' treatment.

The association of various degrees of thyreoid and pituitary insufficiency is often noted in clinical practice.

Diagnosis.

The clinical picture of well-defined cases of myxœdema is so striking that it can scarcely be mistaken for any other condition. A diminution of the basal metabolic rate below −25% and an increase of the blood serum cholesterol over 500 milligrammes per 100 cubic centimetres would be valuable confirmatory evidence of the presence of myxœdema. The final test of the correctness of the diagnosis would be the successful therapeutic administration of desiccated thyreoid substance.

From the history of the patient suffering from menorrhagia two important lessons are to be learnt. In the first place, her condition had been variously regarded as being due either to anæmia (cause not stated) or to jaundice or to nephritis. These are three of the common mistakes in diagnosis. In the second place, it is commonly thought that sufferers from myxœdema are of a stout build. This idea may lead the unwary into error. It will be noted that she was of the tall, thin type, her height being 167·5 centimetres (five feet seven inches) and her weight 52·2 kilograms (eight stone four pounds).

There are certain points of resemblance between chronic nephritis and myxœdema. In both diseases subcutaneous swelling, facial pallor and albuminuria may occur. But the presence of "solid œdema", dryness of the skin and hair, together with mental hebetude, should suggest to the seeing eye the necessity for a therapeutic trial of thyreoid substance.

The association of a type of anæmia resembling pernicious anæmia with myxœdema has already been discussed.

The diagnosis from various types of obesity should present no difficulty. The distribution of the adipose tissue in certain endocrine types of obesity is pathognomonic. The pelvic apron of fat in hypopituitarism (see Figures XII, XIII, XIV) and the broadening of the hips in some patients after the cessation of ovarian activity are distinctive (see Figures XVA and XVB). In acromegaly, enlargement of the skull and hands is typical (see Figures XVIA and XVIB).

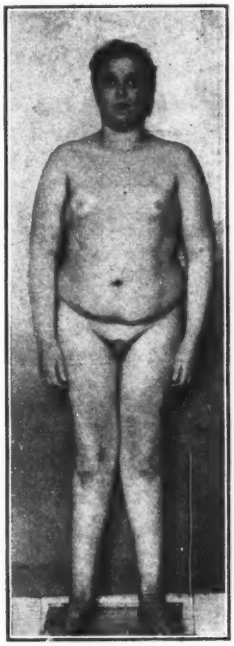

FIGURE XII.

FIGURE XIII.

Prognosis.

As the adoption of thyreoid medication has altered the natural course of the disease, it is very

interesting to read Murray's remarks about the prognosis in untreated cases. He stated that the

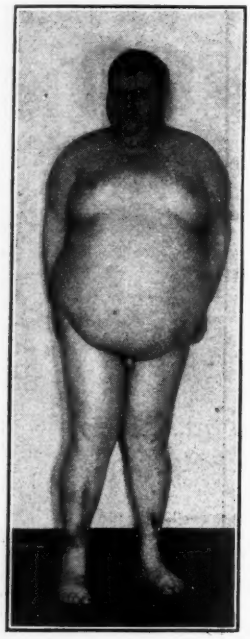

FIGURE XIV.

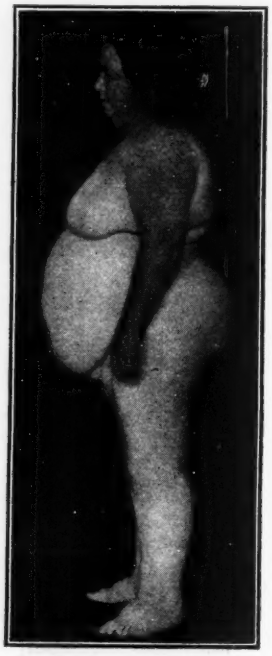

FIGURE XVA.

tendency of the disease was to become progressively worse, but that the course might be slow (13 of 320 patients whose records he collected from various sources lived for more than twenty years), and there might be temporary periods of improvement,

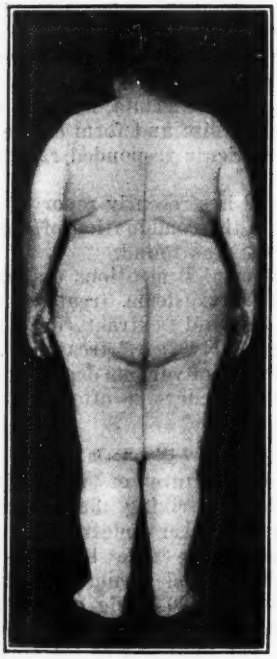

FIGURE XVB.

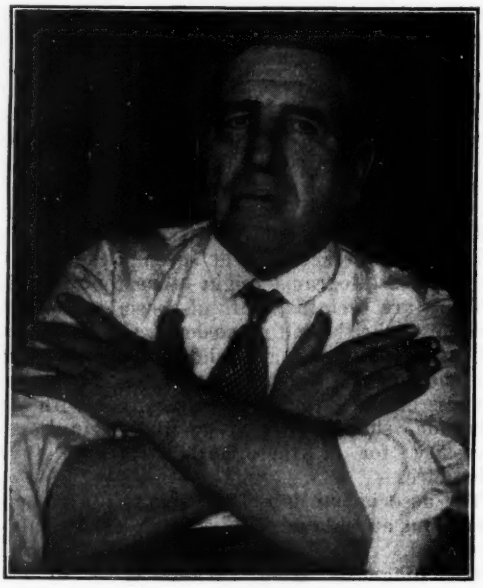

FIGURE XVIA.

especially during warm weather. Death usually occurred from some acute disease, such as influenza or pneumonia, which the patient was unable to resist, or from cardio-vascular and renal degeneration.

The prognosis now depends very largely upon early diagnosis and the application of suitable treatment. Sturgis and Whiting[16] utter a warning about the prognosis in advanced myxœdema with cardio-vascular degeneration or serious mental changes. They emphasize the necessity of giving a guarded prognosis in these cases.

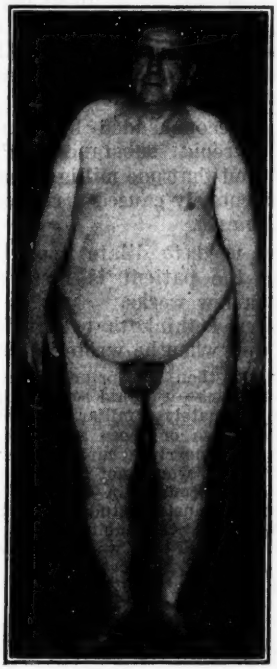

FIGURE XVIB.
Showing acromegaly and hypopituitary pelvic apron of fat.

As there is very little tendency to a spontaneous cure, relapses will occur if the treatment be discontinued. One in four of Sturgis and Whiting's patients suffered a relapse for this reason. The prognosis is therefore better, as a rule, in educated than uneducated people.

In the series of cases of classical myxœdema under consideration, the male patient ceased treatment for a year and therefore had a relapse, but his condition improved again upon resumption of treatment. One of the women patients attended hospital only on two occasions. The oldest patient of the series, who suffered from an advanced form of the disease, manifested very little improvement after three months' treatment and then ceased attendance. Another of the patients, after showing some initial improvement as far as the skin and hair were concerned, refused to take her food and gradually died of inanition. At autopsy it was found that her heart was very small, weighing only 150 grammes (five ounces). No gross lesion was found in the brain, and there was no organic obstruction in the œsophagus. It was considered that her refusal to take food was due to mental changes. It is impossible to say whether these changes were associated with the thyreoid deficiency. The patient with myxœdema following hyperthyreoidism has been under treatment for too short a time to allow of a discussion on prognosis in such circumstances. The remaining patients have all shown great improvement. Thus, six out of eight patients who submitted to regular treatment, have benefited greatly by thyreoid therapy.

Treatment.

The essential part of treatment is the use of thyreoid substance.

As has been stated in the discussion of the diagnosis, the therapeutic use of thyreoid substance may clinch the diagnosis. It is therefore necessary to employ a thyreoid preparation of known potency. Owing to the earlier use of fresh thyreoid gland, it was the custom to standardize the dried substance in terms of the fresh gland, one grain of the dried gland equalling five of the fresh gland. On account of the varying composition of the thyreoid glands obtained from sheep at different seasons of the year and from different pastures, it was found necessary to abandon the standardization in terms of the fresh gland.

As Reid Hunt[17] states:

> Physicians at the present time are about as likely to think of thyroid dosage in terms of the fresh gland as they would of the dosage of morphin in the fresh juice of the poppy.

He showed that the physiological activity of thyreoid preparations as determined by the resistance of mice to acetonitril and by clinical observations was closely parallel to their iodine content. Thyreoid preparations are therefore standardized according to their iodine content.

In the treatment of all the patients studied, the preparation used was the "Tabloid" thyreoid of Burroughs, Wellcome and Company, Limited, which is standardized to contain 0·32% of iodine.

The treatment consists of two stages, the objective of the first being to remove the manifestations of the disease, and of the second to maintain the patient in health. The second stage must be continued throughout the life of the patient. It is estimated that in the treatment of Murray's[18] original patient the thyreoid glands of more than 870 sheep were used in twenty-eight years.

It is both wise and necessary to confine to bed patients suffering from cardio-vascular complications during the first stage of treatment.

As the sufferers from myxœdema are very sensitive to thyreoid medication, and as there is apparently no known method of determining what dose should be used at the commencement of treatment, it is wise to commence with a small dose. The method advocated by H. Gardiner Hill[19] is as follows. The initial dose given is 0·015 gramme (a quarter of a grain) of the desiccated gland, taken once a day for a week. The dose is increased to 0·015 gramme twice a day at the end of the first week, and to 0·03 gramme (half a grain) twice a day at the end of the second week, and later to 0·06 gramme (one grain) twice a day. He states

that this is an adequate maintenance dose and that a larger one is seldom required. It is necessary, however, to judge by results, and no rules can be laid down.

As stated by Sturgis and Whiting,[16] the proper dose is controlled by: (i) the clinical response of the patient, (ii) the basal metabolism, (iii) the resting pulse rate, and (iv) the body weight. One may add that the blood serum cholesterol content is also a valuable guide as to dosage.

In the series of cases of classical myxœdema under consideration the practice was to commence treatment in some cases with "Tabloid" thyreoid (Burroughs, Wellcome and Company, Limited), 0·03 gramme (half a grain) twice a day, and in others with 0·06 gramme (one grain) three times a day, and to increase the dose up to the optimum maintenance dose. In most cases this was found to be 0·06 gramme three times a day. In one case 0·06 gramme once a day was sufficient, but for the man it was necessary to prescribe 0·12 gramme (two grains) three times a day. The oldest patient of the series was receiving 0·18 gramme (three grains) three times a day when she ceased treatment.

While an initial determination of the basal metabolic rate and an initial estimation of the blood serum cholesterol are almost essential, the repeated use of these laboratory methods of investigation is not indispensable in following the progress of treatment. The general condition of the patient and the resting pulse rate are most valuable guides.

When it is difficult to have determinations of the basal metabolic rate made by the Douglas bag method, Gale's formula[20] (pulse rate *plus* pulse pressure *minus* 111 equals basal metabolic rate) may be of assistance.

Sturgis and Whiting found that their patients did best when their basal metabolic rates were maintained at 5% to 10% below the normal. This observation applies to the woman who suffered from menorrhagia (Case 5, Table I) who has been perfectly well from within a short time of the inception of treatment, in spite of the fact that her basal metabolic rate has never been greater than – 13%.

At the beginning of treatment the patients usually lose weight, sometimes as much as 9·5 kilograms (a stone and half) being lost in a few weeks. This weight is later regained and even increased, owing to the feeling of *bien être* engendered by the treatment.

It is wise to advise the patients to cease taking the "tabloids" for one day a week in order to avoid cumulative effects. Administration of the "tabloids" should be discontinued during any acute illness or if any sign of overdosage, such as tachycardia or palpitation, is noticed.

When myxœdema is associated with cardiovascular degeneration complicated by a severe grade of anæmia, the raising of the metabolism by thyreoid substance is apt to cause an excessive increase in the pulse rate, as each unit of blood contains less oxygen than normal. Sturgis and Whiting[16] advise that two or three small blood transfusions (each of 250 to 300 cubic centimetres) should be given in such cases to increase the oxygen-carrying capacity of the blood. Digitalis should also be used.

Attention should be paid to the elimination of gross focal sepsis, and a mixed diet of adequate iodine content, consisting of an abundance of milk, fish, cereals, fruit and vegetables, and a small amount of meat, should be advised. Foods rich in cholesterol, such as brains, ham, bacon, egg yolk and cream, should be restricted.

Thyroxin is recommended by some authorities instead of thyreoid substance. Plummer and Boothby[21] found that one milligramme of thyroxin injected intravenously caused a rise of 2·8% in the basal metabolic rate.

There is no need to dilate upon the results of treatment, as the patient is restored to normal health within a few weeks.

In conclusion, I think that Dr. Hans Lisser[22] put the case well when he wrote in 1922:

> Bearing in mind, then, our principal mission as physicians—to heal the sick—it would seem incumbent upon us all to be most intimately familiar with every diagnostic and therapeutic phase of those maladies for which we have a cure or very nearly a cure. Experience seems to indicate that the time would not be wasted that might be allotted to a small course in the medical curriculum devoted to the intensive study of these particular conditions. For surely the public have a claim upon us to this degree at least, that we should, with practically no exception, recognize and relieve those suffering from curable lesions.

Summary.

1. A short account of various aspects of myxœdema is given.

2. A series of ten cases of classical myxœdema and six cases of atypical myxœdema are discussed. Reference is made to four patients with ill-defined symptoms suggestive of hypothyreoidism and to five patients (two who had suffered from cretinism and three from myxœdema) who were under treatment when first observed.

3. Attention is drawn to the value of blood serum cholesterol estimations in the diagnosis and treatment of myxœdema.

Acknowledgements.

I wish to thank Dr. W. K. Inglis, Director of the Pathological Department at the Sydney Hospital, for permission to publish the photographs taken by Miss V. E. Jones, B.Sc., whom I also thank.

Although some of the cholesterol estimations were done by myself, with the assistance of Dr. Eva Shipton, to whom I acknowledge my indebtedness, a large number were done by Dr. H. S. H. Wardlaw, Dr. E. B. Jones and Dr. Florence Voss, for whose assistance I am grateful. I wish to thank Dr. R. C. Winn for permission to use Figure XIV.

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HYDATID MOLE AND CHORIONEPITHELIOMA: A NEW METHOD OF DIAGNOSIS AND PROGNOSIS.[1]

By BRUCE MAYES, F.R.C.S.,
Brisbane.

THE diagnosis of hydatid mole has been in the past at best a presumptive one. Many facts may point to the probability of a mole, but there has always lacked that piece of unequivocal evidence which would enable the gynæcologist to declare, and act on his diagnosis. More often the unfortunate patient "drags on" in a state of uncertainty as to her fate and in jeopardy of her health over a period of weeks, until she establishes her own diagnosis by the passage of the "tell-tale" vesicles.

The prognosis was even more difficult and more uncertain. It is estimated that 15% of hydatid moles develop that tragedy of pregnancy, chorionepithelioma. This may appear immediately, or, in other words, the mole may be malignant from the onset, or its development may be delayed for nine or even eighteen months after the disappearance of the mole.

In the diagnosis and prognosis of hydatid mole the gynæcologist has recently been furnished with a reliable laboratory aid, which ranks as one of the greatest discoveries in medicine of the last decade.

The discovery that, following on the embedding of the fertilized ovum in the human female, there is the excretion in the urine of a large amount of a substance (called at present the anterior pituitary hormone) led Aschheim and Zondek to elaborate what is known as the Aschheim-Zondek pregnancy reaction (A.Z.R.).

This was described in detail in a previous issue of this journal.(1) Briefly, it involves the injection of a small amount of urine into an infantile female white mouse. The presence of a powerful hormone in this urine produces in one hundred hours characteristic changes in the ovaries and uterus of the mouse.

By these changes one is enabled to make a diagnosis of pregnancy with an accuracy of almost 100% within a few days of the "missing" of the first period. The validity of this test is not a matter for discussion. It has been definitely established by the experience of thousands of cases in all parts of the world.

The object of this article is to point out a further application of the test to the diagnosis and prognosis of hydatid mole.

A hydatid mole is, as an American author has styled it, "a pregnancy gone wrong". It is the wild overgrowth of chorionic epithelium which normally limits itself to the placenta, but which in the mole proliferates, to the detriment and destruction of the ovum for whose nourishment it was originally intended.

The diagnosis of a hydatid mole can be made absolute by a quantitative estimation of the hormone content of the urine.

One cubic centimetre of urine from a normal pregnant woman contains ten mouse units, or, in other words, one litre contains 10,000 units. (A mouse unit is the smallest quantity of urine which on injection into an infantile female white mouse will produce the typical pregnancy reaction of Aschheim and Zondek.)

The urine from a patient with a hydatid mole contains an enormous quantity of the anterior pituitary hormone, one litre containing often 200,000 to 500,000 mouse units. This extreme degree of hormone concentration is extraordinarily characteristic, and really specific for the hydatid mole.

When one speaks of a quantitative analysis, one is apt to give to those not associated with laboratory work the impression that such analysis entails a difficult and perhaps a doubtful procedure. Such is not the case.

A certain amount of experience is necessary in the interpretation of the actual ovarian and uterine changes in the test animal, but just so much as is

[1] Most of the work here reported was carried out during the tenure of the Walter and Eliza Hall Travelling Medical Research Fellowship from the University of Sydney.

necessary to proficiency in any sphere outside the laboratory. The quantitative element of the work is simplicity itself and can be explained in a few words.

Taking a hypothetical case, the patient with five months' amenorrhœa has a uterus reaching to the umbilicus; she has had a slight loss of blood, perhaps only a dirty brown discharge *per vaginam*.

Instead of the usual practice of expectant treatment, unsatisfactory to both doctor and patient, one takes simply an early morning specimen of urine and proceeds as follows. Take three test tubes; into the first place the undiluted urine, in the second urine diluted with distilled water to one part in 50, into the third urine diluted to one part in 100. Each of these three specimens is now used as an ordinary sample of urine, and a pregnancy test performed in the usual manner with each.

If either the "1/50 urine" or "1/100 urine" gives a positive Aschheim-Zondek reaction, the answer is positive for hydatid mole. If a positive Aschheim-Zondek reaction is obtained with the undiluted urine only, then the case is one of an ordinary pregnancy.

In one case of which the author has had experience, the hormone content was so high that $^1/_{520}$ cubic centimetre of urine gave a positive Aschheim-Zondek reaction. More usually the maximum dilutions giving a positive Aschheim-Zondek reaction have ranged from one in 100 to one in 300. On this information the uterus can be emptied immediately.

The above is the story of a typical case, and those who have seen this work will agree that it is a truly fascinating as well as scientific side of obstetrical investigation.

The diagnosis made and the uterus emptied, the most perplexing question arises: "What is the prognosis?" It is in this direction that the Aschheim-Zondek test is of great assistance. In a previous article it has been pointed out that the production of a positive Aschheim-Zondek reaction follows on the formation of chorionic epithelium.

This holds for an abnormal as well as a normal pregnancy. In other words, the growth of chorionic epithelium in the form of a hydatid mole or chorionepithelioma will produce a positive Aschheim-Zondek reaction.

This is, stated briefly, the rationale of the employment of the Aschheim-Zondek test in controlling the prognosis of a hydatid mole.

The usual behaviour of the urine from a case of hydatid mole is that a positive Aschheim-Zondek reaction persists for five to seven weeks following the expulsion of the mole. (In a normal pregnancy the urine fails to react to the Aschheim-Zondek test in ten days after the termination of the pregnancy.)

In controlling the prognosis of a hydatid mole, the author's practice has been to test the urine every week until a negative result is obtained and thereafter at intervals of one to three months.

The return of a positive reaction at any stage indicates either a further pregnancy or the development of a chorionepithelioma. Physical examination of the patient will usually decide this point.

In the few cases so far "followed up" in the various clinics, evidence of the occurrence of chorionepithelioma has been obtained in this way before any symptom or physical sign of such a condition had presented itself.

The value of this laboratory aid in determining the prognosis of a hydatid mole needs no elaboration. Its practicability is its own recommendation. The practice in the past has been to request that the "mole" patient return at frequent intervals for examination. Every doctor knows how frequently this good advice goes unheeded; one submits that a monthly specimen of urine is a request which very few patients would refuse or neglect to supply.

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Reports of Cases.

TWO CASES OF MALARIA.

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Two cases of malaria under treatment at the same time in a public hospital medical ward in Australia is a sufficiently rare occurrence to call for passing notice. For this reason notes are furnished in this communication of two cases of benign tertian malaria revealed in the course of routine laboratory investigation at the Mater Misericordiæ Public Hospital, Brisbane, during April, 1932.

The point of interest in one of the cases was the immediate and dramatic benefit conferred on the patient's condition by combining blood transfusion with quinine. The other case illustrates the transmission of the infection in Australia to a subject who has never been outside the Commonwealth, and also the immediate beneficial effect of quinine medication.

Case I.

The condition of one of the patients in question at one stage occasioned concern. He was G.W.T., an athletic young man of twenty-eight years, a public servant, who had spent, during March, a vacation of a few weeks in New Guinea. He was admitted to hospital on April 3, complaining of bodily pains and perspiring freely. The pain was felt in the left side of the chest anteriorly. He had a cough, but no sputum. He was exhausted and his face was flushed. The abdomen was much distended; respirations were 31, pulse 124 per minute and bounding. The temperature was 39·2° C. (102·6° F.). The apex beat was normally situated. The sounds were good and there was one centimetre of right heart dulness. The pulmonary second sound was a little accentuated. The pulmonary findings were somewhat equivocal. The respirations were bronchial in character in both chests anteriorly. No adventitiæ were heard. The bases of the lungs were not examined on this occasion, owing to the extreme degree of exhaustion present. The spleen was palpable and soft. A diagnosis of pneumonia in the stage of resolution was made and routine treatment instituted. Subsequent percussion revealed a marked dulness at the base of the left lung. On the day after admission the temperature had dropped to 36·1° C. (97° F.), but a rise of temperature

during the same afternoon, and subsequent diurnal rises, ranging between 38·3° and 38·9° C. (101° and 102° F.), raised the suspicion of an unresolved pneumonia, and at the end of the first week of treatment the existence of an empyema was suspected, owing to the maintenance of the remittent temperature. The sweats had persisted. The general condition of the patient was depreciating.

The history, given by the relatives of the young man, was that a week prior to his admission to hospital he had returned from a vacation tour in New Guinea. On the afternoon of the day he had left the ship he had been seized with a rigor at his home. He felt weak, sweated, and after ineffectual home treatment, including rest in bed, came to hospital. Three days after his admission the skin displayed a slight icterus, but by the end of the week it was obvious that he was suffering from a severe anæmia, for the skin was lemon-yellow. On April 8 the left side of the chest was needled, but fluid was not obtained.

On April 11 an X ray examination of the left side of the chest was made. The report was: "Left heart enlargement. The left diaphragm is higher than the right. Otherwise, nothing abnormal detected." A resemblance of the symptoms to those of a boy in the same ward, then recovering from an attack of benign tertian malaria of a mild type, suggested a blood examination in the adult patient.

A complete blood count and examination of the blood for malaria parasites was asked for. The blood film report was as follows:

> Red blood cells 1,960,000, white blood cells 4,000 per cubic millimetre, hæmoglobin value 50%, colour index 1·3. Nothing abnormal was detected in the differential count. Malaria parasites are present. Anisocytosis, slight poikilocytosis and polychromasia are present. Punctate basophilia is seen in a number of cells. A few nucleated red cells are present. Platelets are fairly numerous.

The infection was the benign tertian type. On the evening of April 12 the patient received 0·6 gramme (ten grains) of quinine. Saline solution bowel washes were given on the next day, and quinine in 0·3 gramme (five grain) doses on two occasions. On this day the patient was excitable in the morning, and in the afternoon, following a visit by his relatives, developed acute delirium, which was successfully treated by "Amytal" and the cold pack. During the evening he was restless and made several attempts to get out of bed. During this day his temperature reached 39·3° C. (102·8° F.). On the following day, April 14, his condition improved. He received quinine in 0·12 gramme (two grain) doses every two hours. The extreme degree of anæmia, however, and the patient's general downward course to this date were considered grounds for a blood transfusion, and accordingly this was carried out by Dr. Geaney, assisted by Dr. Cohen, Registrar, on the afternoon of April 14. The patient's brother had been discovered by compatibility tests to be a suitable donor. Sixteen ounces of the brother's blood, transfused by the indirect method, together with six ounces of citrate solution, were given. The patient's condition improved dramatically from this date. The temperature fell immediately, and rose above 37·2° C. (99° F.) once only thereafter during the remaining twenty-five days of his stay in hospital. Quinine medication was continued throughout this period in doses equivalent to 0·12 gramme (two grains) every two hours. Two blood counts, one made on April 26 and the other on May 9, the day on which the patient left the hospital, show the rapid reestablishment of hæmatopoiesis. On April 26 the count was: Red blood cells 2,960,000, white cells 7,500 per cubic millimetre, hæmoglobin value 68%, colour index 1·08. Anisocytosis, poikilocytosis and polychromasia were observed. Malarial parasites were not seen.

On May 9 the count was: Red blood cells 4,310,000 per cubic millimetre, hæmoglobin value 90%, colour index 1·0. There was slight anisocytosis. No parasites were seen.

The clear condition of the chest upon the patient's discharge from hospital seemed to indicate the correctness of the diagnosis of pneumonia, which was the immediate occasion of his admittance.

Case II.

The younger of the two patients was John M., sixteen years of age. He was admitted on April 7 from the outpatient department with a history of malaise for fourteen days. Every second day he "had got cold and shivered and become hot afterwards". He had a pain "down the left side, just over the heart". The pain started "under the left ribs and went up to the heart". He had lost appetite. The apex impulse of the heart was heaving in character, and there was rapid cardiac action. There was nothing in the lungs relevant to a definite diagnosis. Slight tenderness in McBurney's region and upon rectal examination somewhat nearer the mid-line were thought to indicate a subacute appendicitis, and this was the diagnosis made. The tongue was coated. The boy had been staying at Redlands Bay with a friend who had contracted a malarial infection two years before. The boy had been fourteen days with his friend when his own shivers began. During this period the friend had had a recrudescence of his malaria.

On April 7, the day of his admission, the boy seemed depressed. Slight pain in the pericardial region persisted on April 8. The boy said that he had taken quinine for the shivers on April 7. On April 8 the possibility of a malarial infection as a point in the differential diagnosis was suggested by Dr. G. A. McLean. A sample of blood was sent for examination and the parasites of benign tertian malaria were found in it. The red count was unaffected. The boy had a rigor in the ward, lasting almost an hour, on April 9, and on April 11, about the same time in the morning, he had an indication of a rigor. Quinine bisulphate, 0·6 gramme (ten grains) was given every four hours. The temperature dropped at 2 p.m. on this day and remained below 37·2° C. (99° F.) till his discharge on April 19. On April 9 the temperature was raised to 39·1° C. (102·4° F.); the pulse rate was 124 per minute and respirations 34 per minute. After April 11 his convalescence was rapid and uninterrupted.

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I am indebted to Dr. F. C. Bechtel for permission to publish the first case, and to Dr. Ellis Murphy and Dr. G. A. McLean for permission to publish the second.

Reviews.

BLOOD GROUPING.

A TRANSLATION of "Individuality of the Blood", by Professor Leone Lattes, has been issued in the attractive series of "Oxford Medical Publications".[1] The book provides a most up-to-date and long-needed detailed summary of the vast and increasing knowledge of "blood grouping" in all its aspects—clinical, forensic, genetic, anthropological *et cetera*. The scope of the work is best indicated by stating that the bibliography and authors' index occupy nearly ninety-two pages and that on each of these pages there are about twenty-five citations. The author does not, of course, refer to each of these two thousand odd papers, but obviously he has skimmed their cream. The work under review is an English translation of the French edition, but no sign of French idiom can be detected in the freely flowing English exposition. The book is really a credit to author, translator and publisher.

After a short introduction, Chapter II deals with the serology of the subject in seventy-five pages and nothing of importance is omitted. Landsteiner's priority in the discovery of the groups is definitely, if somewhat casually, conceded and that worker's notation of groups O, A, B and AB is recommended for general use instead of the meaningless numerals of the Jansky and Moss systems. Landsteiner's law is taken as the keynote of the whole

[1] "Individuality of the Blood in Biology and in Clinical and Forensic Medicine", by L. Lattes, translated by L. W. Bertie, M.A., B.M., B.Ch.; 1932. London: Oxford University Press (Humphrey Milford). Demy 8vo., pp. 427. Price: 30s. net.

work (page 25), and the theme is again emphasized on page 43: "The fact of belonging to a definite group is a fixed character of every human being, and can be altered neither by the lapse of time nor by intercurrent diseases". The author seems to believe that, on the whole, more evidence is needed of the reality of the subgroups of Guthrie and of Tebbutt. Chapter III, on the hereditary aspect, is a little tedious and would, we believe, have been shortened if Strandskov's (1931) valuable statistical paper had been available at the time of publication. This puts the validity of Bernstein's theory beyond much doubt. Chapter IV is devoted to the ethno-anthropological aspect; it reflects an immense amount of patient research of the literature and thus future workers in this field are placed under a deep debt. Chapter V deals with the clinical application to blood transfusion. A rational discussion of the "universal donor" theory and its implications is given and a commonsense conclusion arrived at (pages 243, 244). Chapter VI takes up the forensic question of paternity and the identity of blood stains. As to the former, we are glad to find support for the opinion long held that grave and lifelong injustice may result from the neglect of courts of law to order, in paternity cases, tests for both iso-agglutinogens and the Landsteiner M and N agglutinins. By the discovery of these, the chance of establishing paternity has been doubled certainly, perhaps trebled. German courts are very enlightened in this matter, believing, probably, that if injustice must be done, an attempt should at least first be made to be just. Chapter VII, on technique, is clear, simple and adequate. An index is provided.

Within its self-imposed limitations, and these are by no means narrow, there are few questions, if any, which this book does not make an honest attempt to answer. If the translation reflects the original, we should say that the author is not only an expert, but that he knows how to demonstrate his subject to the fullest advantage. There have been fewer more agreeable tasks than reviewing his book. No laboratory can afford to be without it, not only for its main matter, but for the profoundly impressive list of papers cited.

The book, as an Oxford Medical production, is, needless to say, well produced.

A TEXT BOOK OF BIOLOGY.

IT may well be said that of the making of text books there is no end. In fact, the compilation of new text books provides one of the few ways of keeping up to date in these days of specialization. We turn, therefore, with some interest to the latest text book of "Biology for Medical Students", by Hentschel and Cook, of London,[1] since zoological text books intended for this stage have not changed much with the passing of the years.

It is stated in the preface that the book is (*a*) primarily intended to cover the biology syllabus for the first M.B. examination of the University of London *et cetera*, and (*b*) that it is more or less unique in combining the two branches of biology—botany and zoology—under one cover. The authors affirm that it is a pity that in many institutions preparation for the biology examination is carried out by separate botanical and zoological departments. If, however, the two sections of this volume are intended to demonstrate that closer contact of the two branches of biology develops some different viewpoint or new method of teaching, the book is a failure. It is just an elementary text book of zoology and a more elementary text book of botany bound up together, with a common introduction to cell structure at the beginning and a joint effort on heredity and evolution as a fitting conclusion.

It is difficult to see how things could be different, unless the subject matter of biology is treated in an entirely different manner from what is usual, and by a single author, or by two who collaborate completely in the writing of each chapter. Since, however, this book is primarily designed for the first M.B. examination of the University of London, its range and mode of treatment are limited at the very outset, for the constituent colleges of that worthy institution work to a rather rigid syllabus. From this point of view the book will no doubt prove very useful for London University students.

Apart from this, the book is very well got up indeed, and is excellently illustrated. Particular mention might be made in passing of the photomicrographs of sections of hydra.

The contents follow the usual lines. After an introduction to the protozoa (Amœba and Paramecium being used as examples) and an introduction to the metazoa (Hydra and Obelia as examples), the earthworm, dogfish, frog and rabbit are discussed in detail as types. A section on the embryology of the frog, chick and rabbit follows, and then we are introduced to the plant kingdom. Two algæ are described, the life history of a fern is discussed, and then follow chapters on plant structure and physiology. The final chapters deal with the malarial parasite, the tapeworm, certain fungi, bacteria, and evolution and heredity respectively.

There are six hundred pages in the book, yet the term insect does not even appear in the index! Since the book is intended for medical students, and since every minute of their long course of training is precious, one might expect far greater attention to types and aspects of biology that have some very special bearing on medicine. Insects play an extraordinary part as vectors of human disease—there are also fungi which are responsible for human disease—they are all more worthy of mention than the details of structure of plant seeds. The section on heredity could easily have been profitably expanded and much other descriptive matter left out to make room.

There are one or two slight errors to be noted. Thus, in the section on malaria it is stated that in tertian and quartan fevers the life cycle occupies three and four days respectively. Actually the period of growth and schizogony occupies forty-eight hours and seventy-two hours respectively.

[1] "Biology for Medical Students", by C. C. Hentschel, M.Sc., and W. R. Ivimey Cook, B.Sc., Ph.D., with Foreword by G. E. Gask, C.M.G., D.S.O., F.R.C.S.; 1932. London: Longmans, Green and Company. Demy 8vo., pp. 630, with illustrations. Price: 18s. net.

HOSTILITY IN MARRIED LIFE.

BOOKS on sex life and marriage are becoming more and more numerous. Some are useful, others are written with an object that is hard to discover. "Sex Hostility in Marriage", by Dr. Th. H. Van de Velde, is useful and is intended for people "whose marriage is menaced by the spectre of hostility".[1] He holds, and rightly, that "a diseased person should not attempt to obtain help from quartan fevers the life cycle occupies three and four days only treatment adapted to his particular condition can be of any assistance. With this we are in entire agreement, and would add that the treatment of a person diseased either in mind or body should be undertaken by a medical practitioner who is *au fait* with his subject.

The book is divided into two parts. The first deals with the origin of hostility in marriage, and chapters are devoted to primary and secondary sexual aversion, the contrast between masculine and feminine and the passing from specific aversion to antagonism in marriage. The second part of the book is devoted to a consideration of prevention and treatment. The chapters in this section are entitled: "Apologia of Marriage", "The Choice of a Partner", "Insight and Adaptability", "The Importance of Practical Erotic Knowledge in Marriage", "Treatment". We think that the author might have laid more stress on the influence of upbringing and on the intellectual environment of the home. The greater part of this book, however, contains sound teaching and would certainly be of use for those for whom it is intended. Medical practitioners need to be careful before they recommend to their patients any book on sex; no exception to this statement can be made as far as this book is concerned.

[1] "Sex Hostility in Marriage: Its Origin, Prevention and Treatment", by Th. H. Van de Velde; translated by H. Marr, M.A.; 1931. London: William Heinemann (Medical Books) Limited. Demy 8vo., pp. 312. Price: 17s. 6d. net.

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POST-GRADUATE WORK.

WHILE medicine is a grateful lover, she is an exacting mistress. Though many woo her, she reveals herself wholly to none, and those who would learn most about her must be constant and whole-hearted in their devotion. She changes her garb and alters her make-up with stealth and often to such good purpose that he who neglects her for a space may feel that he is in the presence of a stranger when he turns to her once more. That the guerdon of service to her will depend on the motives of the servitor and on his qualities of heart and mind need not be discussed at the moment, but it is true of this as of every other love that he who would receive much must give much. The new graduate in medicine soon discovers that he must read. If he fails to read, he finds that those who were his former fellow students soon leave him far behind. Reading, of course, is not sufficient; it must be supplemented by observation at the bedside, in the laboratory, in the operating room and in the *post mortem* room. At the same time, it is surprising how much can be accomplished by systematic reading and how easily the gaps left by systematic reading can be filled in when opportunities for clinical and laboratory observation arise. Conditions of practice in Australia are such that systematic laboratory and hospital study are available to relatively few and the last few years have seen a great increase in the demand for facilities for post-graduate study.

There is no need to dwell further on the need for post-graduate study or to refer to the advantages of attending set courses in particular subjects. In all States of the Commonwealth post-graduate committees exist. There is no doubt that the ideal arrangement is that of a permanent committee which was adopted first of all in Melbourne. New South Wales, the State with the largest number of medical practitioners, has in belated fashion appointed a permanent committee. In a recent issue of this journal the inauguration of the New South Wales Permanent Post-Graduate Committee was announced and its office-bearers were named. Time and time again we have extolled the organization of the Melbourne Permanent Post-Graduate Committee and would point out that by the establishment of a permanent committee continuity of effort is made possible and responsibility is shared by the several organizations from which representatives on the committtee are appointed. There is the added advantage that a committee in control of its own finances is answerable to no one as to how its money is spent and has not to go cap-in-hand to a Branch Council or to some other body to ask for funds.

Although the bodies controlling post-graduate work in the States are well organized, they could be made more useful if their work were coordinated. The ideal to be sought is continuous teaching. This does not imply that the annual refresher courses are unnecessary. On the contrary, they supply a very important need. In several States regular demonstrations available to all medical practitioners are held and these should be extended. The annual refresher courses should be coordinated. It would be well if the committees of the several States arranged their refresher courses so that they were as evenly spaced as possible throughout the year. No two courses should clash. Each committee should, moreover, cater for graduates from other States. Graduates of one medical school would be stimulated if they attended a course conducted by teachers who were graduates of another medical school. When a practitioner leaves his practice for a week or a fortnight to attend a post-graduate course, it will be immaterial to him whether he

travels one, two or three hundred miles to reach his destination. Each large centre in Australia has capable teachers who by the force of their personalities could create a lasting impression on the minds of graduate students. The interstate jealousies of a decade or two ago are non-existent and the migration of graduates from their own State to a refresher course in another would create a healthy rivalry to supply the needs of graduates. Since more will be expected of States possessing a medical school, we would suggest that, to begin with, the committees in Melbourne, Adelaide and Sydney should confer with this object. Later on all the States might cooperate. If steps such as these were taken, there would eventually emerge a central advisory council for post-graduate work. A central council could not only coordinate State activities, but would be able to arrange for more frequent visits of overseas lecturers.

Current Comment.

OTOMYCOSIS.

NUMEROUS common diseases are known to be caused by fungi of various kinds. Probably there are many that have not yet been recognized as mycotic. At any rate it seems quite certain that of the multitudinous species of fungi there are many pathogenic species unknown even to the few experts in medical mycology. Castellani has compiled an imposing list, which grows larger and more complex every year.

Otomycosis is a fungous disorder of the external auditory canal, well known to aural surgeons and to medical practitioners in tropical countries. Various species of fungi may be concerned in the ætiology of this condition, and there are numerous clinical manifestations; the term otomycosis is thus a loose one, and its application a confession of ignorance. King Gill prefers the name *otitis externa mycotica*, which is more exact anatomically, but otherwise scarcely preferable to the older term.[1] In his introduction Gill remarks that microscopic fungi were studied and investigated as long ago as the year 1677, that is, long before bacteria were recognized. This fact makes it all the more remarkable that so little comparatively has been learnt of fungi in their relation to disease.

Gill states that about ten different species of fungus have been found growing in the ear: the commonest are probably *Aspergillus fumigatus* and *Aspergillus nigrescens*. The conditions predisposing to otomycosis are maceration due to the entry of water into the ear, injury by foreign bodies, pyogenic infection, a tropical or subtropical climate, individual susceptibility. According to Castellani, the fungus produces a toxin that causes inflammation and serous exudation, which may be followed by pyogenic dermatitis and, perhaps, later by an eczematoid condition of the external auditory meatus. The commonest symptom is itching in the external canal; this may become almost unbearable. If the fungus grows profusely, the canal may be filled up and the patient complain of fullness in the ear and obstruction to the passage. Tinnitus and deafness may occur. Scales, crusts and fissures may be formed, and pyogenic infection may be introduced. Sometimes the drum is invaded; it may be perforated. Gill points out that diagnosis is usually easy, but the condition is often overlooked. The most important diagnostic factor is the finding of the fungus in a smear made from material in the ear. Confirmation is obtained if the fungus is cultured on Sabouraud's agar or Raulin's liquid medium. It is important to keep the inoculated media for two weeks or more, as fungi grow relatively slowly under artificial conditions.

The main factors in treatment are mechanical cleansing of the external auditory canal, reduction of local inflammation, and the limitation of sporulation. Care should be taken to avoid trauma to the canal. Endeavours should be made to restore the parts so nearly to normal that recurrence is unlikely. There is no specific cure; numerous antiseptics have been used from time to time. Gill remarks that thoroughness is the first essential to success in treatment, and dryness is necessary for the prevention of recurrence.

Probably otomycosis is much commoner in Australia than is generally supposed; certainly it is by no means rare in Australia's tropical dependencies. As warm weather, bathing and trauma are factors in the causation of the disease, it might be supposed that surf-bathers should be commonly affected. An investigation should be of interest and value. Mycology has been undeservedly neglected by medical practitioners.

[1] *Archives of Otolaryngology*, July, 1932.

MAGNESIUM DEPRIVATION AND RENAL DISORDER.

DURING recent years extensive investigations have been made concerning the effects of various diets on renal function and structure, and more particularly the results of excessive protein intake. W. Cramer has recorded his observations on the experimental production of kidney lesions by diet.[1] His original intention was to study the biological effects of a mineral imbalance between magnesium and calcium ions, which are known to display mutual antagonism. In his experiments on rats kept on synthetic diets, in which the proportions of inorganic salts in the salt mixture were varied to produce imbalance, it was found that degenerative lesions in the renal glomeruli and tubules followed the omission of magnesium salts.

[1] *The Lancet*, July 23, 1932.

The synthetic diet was that used in routine vitamin investigations, consisting of white light casein, wheaten starch, fat and inorganic salt mixture. In some the fat used was cod liver oil (with or without olive oil) and a little added marmite. In others butter was given without marmite or yeast. The diet used contained 0·632 milligramme of magnesium in 100 grammes. In the control experiments magnesium sulphate was added to the salt mixture. No attempt was made to remove all magnesium from the diet, as one object was to observe the effect on tumour growth of disproportion of certain inorganic salts. It was necessary to preserve the animals over long periods in good health. For six weeks the animals looked and grew as well on the diet with the magnesium-free salt mixture as on the control diet, and the temperature remained normal. When they were killed, nutrition was good and all the organs seemed normal, except the kidneys, which were enlarged, with puckered surface and sometimes grey mottling. Striation was seen on section at the junction of medulla and cortex. There was extensive degeneration of the glomeruli and tubules; this extended far into the cortex, but was most marked at the junction of medulla and cortex. There was no evidence of inflammatory reaction, but increase of connective tissue was noted sometimes round the degenerated tubules. Sometimes (not always) were found calcareous deposits in the tubules and glomeruli, generally absent from the more peripheral parts of the cortex and almost confined to the junction of the cortex and medulla. Albumin was found in considerable amount in the urine of rats after they had been taking the magnesium-free salt mixture for four or five weeks. In the control rats albuminuria was absent or found only in traces. Every rat kept for five weeks on the diet with magnesium-free salt mixture exhibited extensive degenerative renal lesions. On the control diet about half the rats showed some degenerative renal lesions, but much more restricted in extent and limited to the junction of cortex and medulla. Such lesions consisted almost entirely of calcification in the tubules.

Thus there appeared to be some factor, apart from the absence of magnesium from the salt mixture, which, with a synthetic diet, could induce degenerative changes, though more limited and of different kind. To eliminate the occurrence of this limited calcification in the controls, the diet was changed in various ways, but in only one with success. To supply vitamin *A*, cod liver oil was given in most of the experiments. It was deemed possible that the presence of vitamin *D* in this oil was the factor determining the degeneration and calcification, albeit the amount of cod liver oil was only moderate. The oil was replaced by butter, and, in this series, kidney changes were absent from control animals receiving magnesium, but animals deprived of magnesium salts showed extensive degenerative changes.

H. D. Kruse, E. R. Orent and E. V. McCallum kept rats on a diet containing only minimal traces of magnesium (0·018 milligramme per 100 grammes). On this diet, as early as the third to the fifth day the rats showed hyperæmia and vasodilatation of the skin. Between the eighteenth and twenty-third days violent convulsions and other pathological phenomena occurred. In Cramer's experiments the kidneys seemed selectively implicated and the animals remained normal in appearance, growth and nutrition. It was expected that diminution of the intake of magnesium ions would lead to a preponderating effect of calcium ions and would produce more extensive renal calcification than actually occurred. The degenerative changes were unexpected. They show that experimentally degenerative changes may be caused by dietetic measures not involving the introduction or formation of toxic substances. Apparently the mineral imbalance specifically affects the renal tubules and glomeruli. Clinically the administration of large doses of magnesium sulphate in solution by mouth or rectum has been of signal benefit in the hæmorrhagic nephritis of children to ward off or alleviate uræmic convulsions. In comatose patients or those actually suffering from convulsive twitchings, intramuscular injection of a 25% solution (0·2 mil per kilogram of body weight) is advised. Magnesium sulphate produces a fall in blood pressure and cessation of cerebral symptoms. Massive doses do not produce diarrhœa in children with hæmorrhagic nephritis.

In this connexion it might be noted that magnesium sulphate injected intravenously or intramuscularly reduces irritability of the intestine and arrests peristalsis induced by physostigmine or barium. Magnesium salts are purgative only when administered by the alimentary canal. When they are administered by mouth, with efficiently acting kidneys, excretion is very rapid and not enough accumulates in the blood under normal conditions to exert any special action. Absorption from the bowel is very slow. Excretion is mainly by the kidney, only traces being eliminated by other organs. Renal excretion is very rapid, almost all the drug absorbed appearing in the urine within forty-eight hours. By "salt action" magnesium in its excretion by the kidneys renders the urine more abundant, thus being diuretic. The excretion of magnesium is attended by increase in the calcium in the urine, while the calcium of the fæces may diminish. Injected by the subcutaneous or intravenous route, magnesium salts in sufficient quantity produce anæsthesia and narcosis and eventually death from respiratory paralysis, by direct action on the central nervous system. In this regard calcium is again antagonistic. Applied to nerve trunks in 25% solution magnesium salts act like cocaine, first paralysing the afferent and later efferent fibres. Injected subdurally, they induce anæsthesia in the areas below. Investigations such as Cramer's help to elucidate the pharmacology of magnesium, but the mechanism of the action of magnesium sulphate (other than as an aperient) is not yet thoroughly understood.

Abstracts from Current Medical Literature.

PHYSIOLOGY.

Histamine and Gastric Secretion

J. SACKS, A. C. IVY, J. P. BURGESS AND J. E. VANDOLAH (*American Journal of Physiology*, July, 1932) describe a method of extracting histamine from the pyloric mucous membrane of hogs. The activity in stimulating gastric secretion of all fractions from the original acid extract to the final crystalline histamine ran parallel with the vaso-depressor effects. Histaminase, when injected subcutaneously, destroys the factor in pyloric extracts which stimulates gastric secretion. The authors consider that presumptive evidence has been obtained that "gastrin" is either histamine or a closely related iminazole derivative. Pilocarpine and isopilocarpine are the only derivatives so far tested which are effective, and comparatively large doses are required. As iminazole derivatives are known to be present in the urine, the authors attempted to obtain an excitant of gastric secretion from this source. In one experiment of three the material obtained from one litre of urine produced an increase in gastric secretion.

Heat Loss.

BY recording the blood flow in the limbs by a calorimetric method G. W. Pickering (*Heart*, Volume XVI, 1932) has studied the effects on the cutaneous circulation resulting from local cooling or warming of other parts of the body. It appears that the mechanism controlling heat loss from the skin by alterations in the calibre of the cutaneous vessels is of a dual nature. First, the application of cold causes reflexly a cutaneous vasoconstriction which is immediate in onset and which passes off in the course of some ten minutes. No corresponding reflex vasodilatation has been observed to follow the application of heat to the skin, but if the heat stimulus be excessive in intensity, reflex vasoconstriction may occur. Such cutaneous vasoconstriction has been observed by other workers as a result of the application of strong stimuli of varied character; heat, cold, pain and loud noises may all give rise to the same effect. The absence of reflex dilatation of the skin vessels would seem to indicate that the central reflexes elicited from the skin are chiefly concerned with the immediate protection of the body against cold. Following the reflex action of cold stimuli there occurs a persistent vasoconstriction which is produced by a central action of the cooled blood leaving the areas to which the stimulus has been applied. Heating an area of the skin causes a similar central effect, resulting in vasodilatation. Introduction of hot or cold water into the stomach produces the same effects in the cutaneous circulation by raising or lowering the general tissue fluid temperature. A simple calculation indicates that the sensitiveness of the central mechanism is such that a change of tissue temperature of 0·025° to 0·05° C. is adequate to produce the characteristic cutaneous vascular reaction.

Blood Pressure and the Splanchnic Nerves.

THE effect of section of both splanchnic nerves in anæsthetized cats has been studied by M. Kremer and Samson Wright (*Quarterly Journal of Experimental Physiology*, March, 1932). When the cardio-aortic and carotid sinus nerves are intact, there occurs a small fall of blood pressure, usually less than 15% of the previous value. This slight fall is accompanied by a marked vasodilatation in the splanchnic area. It has been shown, however, that a compensatory vasoconstriction probably occurs in other regions of the body, including the skeletal muscles. The authors suggest that the vasomotor control of the vessels of the skeletal muscles is of greater functional significance than is generally considered. When the buffer nerves are inactive, the fall is greater, and usually exceeds 50%. This is not the result of the higher initial pressure, and indicates that the buffer nerves protect the organism against excessive fall in blood pressure as well as against a rise. The fall of pressure is diminished by the integrity of one pair of buffer nerves and to a less extent by one intact sinus nerve, while one intact cardio-aortic nerve alone is comparatively ineffective. If the animal is decerebrated, the section of the splanchnic nerves causes an extensive fall in pressure, even with the buffer nerves intact. After splanchnic section the cardio-aortic nerves still exert an inhibitory tonic action, as shown by a rise of pressure following vagal section. Traction on the carotid arteries lowers the pressure in animals in which the vagi and splanchnic nerves are both divided.

The Duodenal Mucosa and the Internal Secretion of the Pancreas.

N. B. LAUGHTON AND A. B. MACALLUM (*Proceedings of the Royal Society*, June, 1932) have investigated the effect of an acid alcohol extract of duodenal mucosa on the blood sugar of rabbits and dogs. The work was carried out to test the claim made by Moore, Eadie and Abram in 1906, that such extracts contained a hormone which excited the internal secretion of the pancreas and which caused the urine of some diabetic subjects to become sugar-free. This recent investigation indicates that duodenal extracts are without effect on the blood sugar level of normal animals, but if administered subcutaneously before the intravenous injection of 0·5 gramme of glucose per kilogram of body weight, prevent the development of the prolonged hyperglycæmia which otherwise ensues. The extracts also reduce considerably the degree of hyperglycæmia following the injection of adrenaline. In partially depancreatized dogs administration of the duodenal extract controls the rise in blood sugar induced by giving glucose by mouth. When the duodenal extract is given by mouth, it has the same effect on alimentary hyperglycæmia as when it is given subcutaneously. Daily administration of the extract over a period of seven to ten days results in a persistent effect on artificially induced hyperglycæmia for two weeks following the last injection. In totally depancreatized animals the extracts are without effect. It would appear from these results that a substance distinct from insulin can be extracted from the duodenal mucosa and that this material exerts its action on the level of the blood sugar by stimulating the cells of the islets of Langerhans to secrete insulin.

The Peripheral Action of the Australian Snake Venoms.

C. H. KELLAWAY AND H. F. HOLDEN (*Australian Journal of Experimental Biology and Medical Science*, September, 1932) present evidence that the venoms of all the common Australian snakes exert a curare-like action on the isolated nerve muscle preparation of the frog. This action is more difficult to demonstrate in the intact frog. Like curare, the venoms cause a marked increase in the chronaxie of muscle. No data are available for the chronaxie of the nerves of the preparations, but the rheobase for both nerve and muscle was increased as a result of the action of the venoms. The venoms which have a marked effect on the irritability of muscle, also cause an increase in the imbibition of water which occurs when the muscle is immersed in Ringer's solution, while those that exert but a slight effect on irritability are without action on the extent of imbibition. There is a definite parallelism between the direct action of venoms on frog muscle and their hæmolytic action on mammalian erythrocytes.

C. H. KELLAWAY, R. O. CHERRY AND F. E. WILLIAMS (*ibidem*) report an investigation of the curarizing action of a number of venoms on the cat and rabbit. The action potentials in the phrenic nerve were used as an indication of the activity of the respiratory mechanism in the central nervous system and it was found that impulses continued to pass down the nerve after failure of respiration as a result of the injection of venom. At the same time stimulation of the phrenic nerve showed that curarization of the diaphragm was partial or complete. The respiratory failure, which is the cause of death, is therefore to be attributed to the peripheral paralyzing action of the venoms. Direct application of venom to the floor of the fourth ventricle caused an increase in the rate and depth of respiration. This effect may be caused

by a local vasoconstriction due to the direct action of the venom on the vessel walls.

BIOLOGICAL CHEMISTRY.

Starvation Ketosis.

HARRY J. DEUEL, JUNIOR, AND MARGARET GULICK (*Journal of Biological Chemistry*, April, 1932) have shown in a series of experiments that a much greater ketosis develops during fasting in the female than in the male. This was indicated not only by the greater excretion of acetone bodies in the urine, but by the greater fall in the carbon dioxide combining power of the blood. A decrease in nitrogen excretion from the control level, followed by a later increase, was found to occur in both sexes. The decrease which is supposed to be traced to the sparing action of the glycogen still remaining in the tissues seemed to be more prolonged in the male subjects. In none of the eight subjects on whom three or more fasting experiments were carried out, was there any indication of an habituation to fasting. The acetone excretion in the last were essentially of the same magnitude as those in the first fasting periods. Obesity was found not to be a predisposing cause of acidosis. However, two subjects who started fasts in extremely poor nutritional condition excreted only insignificant amounts of acetone bodies, as compared with later fasting periods which they began in a far better nutritional condition.

The Basal Metabolic Rates of Vegetarians.

GLEN WAKEHAM AND LOUIS O. HANSEN (*Journal of Biological Chemistry*, July, 1932) have attempted to determine whether long periods of vegetarianism could be shown to have any consistent effect upon average basal metabolic rates. All subjects used in this investigation were at least up to the normal averages in physical health, strength and endurance, as well as in mental intelligence and alertness. The average basal metabolic rate of twenty life-time vegetarians was found to be 11% below that of the Du Bois normal standard, and the study of a large group of long-time vegetarians indicated that a period of from six to eight years of vegetarianism is usually required to produce this effect. This requisite long period of time eliminates the possible influence of differences in digestibility, absorption *et cetera* in the observed results. It is tentatively suggested by the authors that perhaps the cells of the organism, confronted over a long period of time with a low supply of amino-acids, gradually adjust their metabolic processes in such a way as to increase the mechanical efficiency of the body as a heat engine and thus to enable the organism to carry on its normal functions with less loss of the total potential energy of the food in the form of heat.

Iron Retention by Women During Pregnancy.

CALLIE MAE COONS (*Journal of Biological Chemistry*, July, 1932) has presented data for twenty-three iron balances on nine women at different stages of pregnancy. With the usual home diets the daily intake of iron ranged from 9·69 to 19·45 milligrammes. The retention varied from +0·88 to −6·97, with one exception; in this instance there was a negative balance of −2·21. Under fairly ideal conditions of diet and well-being, it seems possible for the maternal organism to assimilate during the period of pregnancy enough iron from food to supply the new-born infant with the needed reserves. The quality as well as the quantity of iron intake, the physiological demands of pregnancy, and also slight upsets in digestion seemed to be important factors in iron retention. Throughout this work every precaution was taken to avoid any contamination with iron through chemicals and during collection of the specimens. The methods are described in detail.

The Need of the Body for Certain Unsaturated Fatty Acids.

EXPERIMENTS with high fat diets in which saturated fatty acids furnish the sole source of energy have been carried out by Herbert M. Evans and Samuel Bepkovsky (*Journal of Biological Chemistry*, April, 1932). They found in a series of experiments that animals do not thrive on diets containing the essentials hitherto known (adequate amounts of protein, all the known vitamins and the essential inorganic constituents) but in which the energy requirements are met by the glycerides of saturated fatty acids. The authors found that when the glycerides of saturated fatty acids were fed as the sole source of energy, they did not at any time promote growth in the rat equal to that obtained with sucrose as the sole source of energy. Unsaturated fatty acid preparations containing fatty acids with more than one double bond were found definitely to lessen the deficiency of the diets. Oleic acid, freed of double bond fatty acids, produces a very slight response, whereas linoleic acid produces a definite response.

Fatty Acids and Nutrition.

GEORGE O. BURR, MILDRED M. BURR AND ELMER S. MILLER (*Journal of Biological Chemistry*, July, 1932) have continued their studies of natural fatty acids in regard to their abilities to cure the deficiency disease in animals caused by lack of fatty acids in the diet. Both linoleic and linolenic acid were found to be effective in curing rats suffering from fat deficiency. In all cases in which the acids were effective, the skin cleared and the condition of the rats was generally improved. A better muscle tone was also noticeable after the rat had been cured. Linolenic acid and linoleic acid were found to be about equal in value and to be able to replace each other in the tissues. Purified oleic acid was found to be ineffective in the curing of sick rats and has been definitely grouped with the saturated acids as ineffective in the curing of rats subnormal because of the lack of fats. This finding substantiates the arguments previously put forward that it is possible for animals to synthesize large amounts of fat from carbohydrate and still to suffer from fat deficiency. An isomer of linolenic acid, α-eleostearic acid, is also ineffective in curing sick rats; the authors suggest that this is due to its high melting point. Tung oil, like butter, was found to have enough undetermined unsaturated acids to effect slow cures. Mixtures of linoleic and linolenic esters were found to be no more effective than either of the esters alone, while the addition of a preparation of methyl arachidonate had a slight unexplained depressing effect.

Deposition of Fat.

L. L. REED, W. E. ANDERSON AND L. B. MENDEL (*Journal of Biological Chemistry*, May, 1932) have continued their studies on the deposition of fat in rats. They present data dealing with the effect of complete ovariectomy and of the administration of thyroxin. The animals experimented upon were given a ration rich in cod liver oil. The animals were subjected to ovariectomy at an age of between three and four weeks; they were killed between seven and fourteen weeks later. The percentage fat content of the bodies of these animals presented a negligible difference when compared with that of intact animals. The animals without ovaries stored a smaller proportion of fat in the genital tissues and a larger proportion in the subcutaneous layers than did the intact animals. The quality (iodine number) of the subcutaneous fat was not altered by ovariectomy. In one group of animals, each weighing one hundred grammes, a daily dose of thyroxin was gradually increased from 0·5 to 2·0 milligrammes. To animals of another group, each member of which weighed two hundred grammes, daily doses of two milligrammes of thyroxin were given from the beginning of the test. In both groups the distribution of the fat was similar to that of the rats that did not receive thyroxin. The percentage content of depôt fat in the entire body of rats which received thyroxin, was less than one-half of that found for the control animals. Moreover, the depôt fat produced by rats receiving thyroxin was more unsaturated, as determined by higher iodine values, than the fat yielded by rats not receiving thyroxin. Of all the factors so far studied by the authors, the character of the diet and the thyreoid hormone represent the only influences that have appreciably altered the quality of depôt fat.

British Medical Association News.

SCIENTIFIC.

A MEETING OF THE SECTION OF MEDICINE OF THE NEW SOUTH WALES BRANCH OF THE BRITISH MEDICAL ASSOCIATION was held at the British Medical Association House, 135, Macquarie Street, Sydney, on September 15, 1932, DR. C. B. BLACKBURN, the Chairman, in the chair.

Myxœdema.

DR. E. H. STOKES read a paper entitled: "Myxœdema" (see page 589).

DR. SINCLAIR GILLIES offered his hearty congratulations to Dr. Stokes on his comprehensive and able paper. He also wished to condole with Dr. Stokes. The amount of work that he had carried out, and the standard of the work, demanded a larger audience. Dr. Gillies thought that the paper should have been read before a meeting of the whole Branch, rather than the Section of Medicine; the man before whom the early case came was the general practitioner, and it was to him that the information obtained in Dr. Stokes's paper should be available. Dr. Gillies thought that the Section should have arranged for greater publicity.

Dr. Gillies had looked up the records of eleven cases of myxœdema seen in his private practice and had concluded that Dr. Stokes had said practically all that there was to be said on the subject. There had been one man only in his series. It was of interest to note that two of his patients had come to him from laryngologists, whom they had consulted on account of some impairment in the voice. One of the patients had been a nun, whose thickened lips, cheeks and nose and puffy eyelids had been typical of myxœdema; the remarkable feature had been that the myxœdematous appearances had ceased abruptly at the site of the band of her veil; the covered portion of her face, her forehead, her ears, and the back of her neck had been normal, and her hair had been fine and normal; her hands had been large and typical of myxœdema. The question arose whether the actinic rays had anything to do with the sites at which the changes occurred. Dr. Gillies stressed the necessity for "spot" diagnosis of myxœdema; if the patient was not recognized as myxœdematous when he first presented himself, his condition might remain undiagnosed for years. A patient had been sent to Dr. Gillies with her mother from a medical practitioner in the country; he had noticed that the mother was myxœdematous, and sent a note back to her medical adviser, suggesting that the mother should be treated. The medical practitioner in the country had replied to the effect that his predecessor in the district had recognized that the woman was myxœdematous many years before and had commenced treatment, but had ceased on account of the alarming symptoms that had ensued on the administration of 0·09 gramme (one and a half grains) of thyreoid extract per day; she had received no further treatment from that time. Dr. Gillies asked why these patients were so susceptible to thyreoid extract. He thought Dr. Stokes had perhaps erred a little on the generous side in the matter of initial dosage; in his experience the initial dose should not exceed 0·03 gramme (half a grain) a day. He remarked that sometimes œdema occurred during treatment with thyreoid extract without any evidence of cardiac involvement; this disappeared when the administration of thyreoid extract was discontinued. He mentioned the occurrence of pains in the joints, and remarked that two of his patients had complained of muscular cramps. The maintenance dosage of thyreoid in his cases had varied from 0·06 gramme (one grain) to 0·42 gramme (seven grains) per day; the average had been 0·18 gramme (three grains). An intelligent patient could practically decide for himself the amount he required.

Dr. Gillies had seen two myxœdematous patients suffering from menorrhagia; both had improved as a result of treatment.

As myxœdema could be so well controlled by the administration of thyreoid extract, Dr. Gillies thought that there was no necessity to enforce any dietary restrictions. The number of daily doses of thyreoid extract might be a point of importance; if patients were given a dose night and morning instead of three times a day, they would be more likely to continue treatment.

In discussing the expectation of life of myxœdematous people, Dr. Gillies mentioned that he had seen an eccentric woman, aged sixty years, who had been suffering from hypothyreoidism or anæmia and who had disappeared before investigations could be completed. He had not seen her again until fifteen years later, when she had developed the appearances of typical myxœdema.

Two of Dr. Gillies's patients had had enlargement of the thyreoid gland. He had seen most of his patients before the estimation of the basal metabolic rate had come into vogue; the figure had been −18% in the three cases in which an estimation had been carried out.

DR. A. W. HOLMES À COURT expressed his thanks to Dr. Stokes for an interesting and instructive paper on a matter of great clinical importance. All would agree with Dr. Stokes that frank myxœdema was very rare; but he thought that subthyreoidism was not so rare as was usually thought. Dr. Holmes à Court remarked that it was strange how persons with well marked signs of myxœdema could walk about for many months and remain unrecognized as myxœdematous. In the previous few months he had seen a patient who had consulted no less than five ophthalmic surgeons on account of thickening of the lids. The patient had been very disheartened and had informed him that numerous procedures, even operation, had been suggested for the relief of the condition. The cause of the trouble had been myxœdema. Perhaps this was an illustration of a too narrow specialization.

Retrogression to myxœdema following subsidence of hyperthyreoidism was of great clinical interest, as sometimes signs of hyperthyreoidism and hypothyreoidism were seen together. This gave cause for wonder how far the estimation of the basal metabolic rate could be used as an index of the vagaries of the thyreoid and its function. He agreed with what Dr. Gillies had said concerning the remarkable sensitiveness of myxœdematous people to thyreoid extract.

Dr. Holmes à Court mentioned in regard to the mental state of myxœdematous persons, that he had noticed that they were of secretive turn of mind and apt to be suspicious. In conclusion, he thought that there was very little to be said, as Dr. Stokes had dealt with the subject so thoroughly.

DR. P. FIASCHI said he was interested in the question of one of the forms of treatment included by Dr. Stokes, that of transplantation. He had seen Professor Kocher do some transplantations in Berne many years previously, and the distinguished surgeon spoke well of the results.

Dr. Fiaschi said his experience in transplantation was limited to one case only, but it was of interest. The case was of a man with urethral stricture, but who obviously had well marked myxœdema. This man had been operated on some years previously by a prominent Johannesburg surgeon and had had an ileo-colostomy done for colitis. After his stricture had been dealt with, it was proposed to the patient to have a transplantation of the thyreoid performed, which he accepted. Accordingly, Dr. Thomas Fiaschi's collaboration was secured. After a partial thyreoidectomy on a young woman at the Sydney Hospital, the excised portion of thyreoid was placed in saline solution and taken to the private hospital in which the man was ready for operation. Here the operation of transplantation was performed according to the technique laid down by Professor Kocher. A small piece of the excised thyreoid gland, about twice the size of a pea, was put in between the left *rectus abdominis* muscle and its posterior sheath in the upper third; another similar piece between the anterior sheath and the rectus muscle. A third piece was placed in the medullary cavity of the upper third of the left tibia, through a small trephine opening, the button of bone being replaced. This man did well and recovered from the symptoms of myxœdema and was able to lead an active business life for some two years. He then

died of general peritonitis, following leakage of the bowel where a malignant growth had occurred at the point of anastomosis of the ileum and colon. A limited *post mortem* examination was done and a search made for the two pieces of thyreoid in the left rectus area, but they could not be located. The left tibia could not be investigated.

DR. ALLAN S. WALKER remarked that Dr. Stokes's paper was an excellent contribution. It was a great mistake to think, because a condition was well known and readily recognized, that it did not merit discussion.

In the first twelve months of his practice he had seen three patients suffering from extreme degrees of hypothyreoidism. One had died of cerebral hæmorrhage, another, a cretin, had also died of cerebral hæmorrhage; the third had improved as the result of the administration of thyreoid extract.

In the previous few weeks he had seen in a suburban hospital another patient who was moribund from circulatory failure associated with extreme myxœdema. This patient had been untreated for many years. It seemed incredible that such people should be abroad in the community with extreme and untreated thyreoid insufficiency. He thought that Dr. Gillies was right in his remark that if the medical practitioner did not recognize the disease the first time the patient consulted him, he would not recognize it at all. This was a matter of clinical acumen, which should be studied, as there was a danger of its fading out in these days when so much reliance was placed on various laboratory procedures. The basal metabolic rate was only one aspect of the subject, and Dr. Walker would never let it cloud his judgement.

Dr. Walker mentioned that he had seen recently, in the Royal Prince Alfred Hospital, a patient who had complained of impairment of her voice. He had asked a laryngologist to examine her. The laryngologist had confirmed Dr. Walker's opinion that the patient was myxœdematous. It was pleasing to receive diagnostic confirmation from a man who saw the condition from a different angle.

Dr. Walker remarked that some patients who had become hypothyreoidic after operation for hyperthyreoidism, were very sensitive to thyreoid medication. It seemed difficult to relieve these people, as some of them seemed unable to tolerate sufficient thyreoid extract to satisfy their lack of it.

He thought Dr. Stokes was to be congratulated on the way he had marshalled his material and presented the photographs and the details of his investigations.

DR. ROBERT S. STEEL expressed his thanks to Dr. Stokes for his excellent paper. He wished to add a word on the pathology, or rather, the chemistry of the œdema of myxœdema. It had been found that the fluid contained 2% of protein, much higher than the percentage of protein in the fluid of cardiac and renal œdema. There was a point concerned with muscle tone that might be of importance in diagnosis; this was the interesting condition of the knee jerk in myxœdema. The slowing down of the metabolism was reflected in the knee jerk, which was much slower than normal. Diagnosis of myxœdema in the thin type of patient might be facilitated by a recognition of this characteristic. Dr. Steel mentioned that he had read of a case in which hypersensitiveness to thyreoid extract had apparently been overcome by the simultaneous administration of iodine; this combination appeared to bring the patient to a better state of equilibrium.

He differed from Dr. Gillies in his views regarding diet. Plummer had shown that œdema would appear in complete myxœdema when the basal metabolic rate fell to −18% or −20%. Dr. Steel mentioned experiments on thyreoidectomized swine, which, if fed on ordinary diet, became œdematous, but if fed on a diet low in protein and rich in carbohydrate, did not become œdematous.

DR. T. M. GREENAWAY said that Dr. Hansman had remarked to him that he was in the habit of performing a Wassermann test on all patients suffering from myxœdema. His impression was that Dr. Hansman believed that the result of the test was more often positive than was usually thought. Dr. Greenaway thought that syphilis might sometimes be a factor associated with myxœdema that proved obstinate to thyreoid therapy. He also mentioned that in one case hypersensitivity appeared to have been overcome by the administration of vitamin *D* in the form of "Radiostol". This might have been due to associated parathyreoid dysfunction.

DR. F. H. WILSON remarked that Dr. Hansman had also drawn attention to the value of vitamin *D*, which was now recognized to have an effect similar in many respects to that of parathyreoid hormone. Dr. Gillies had mentioned the occurrence of muscular cramp; perhaps this had been a manifestation of hypoparathyreoidism.

DR. C. B. BLACKBURN expressed his appreciation of Dr. Stokes's paper and regretted that the attendance at the meeting was so small. Dr. Stokes had not mentioned the liability of hypothyreoidic patients to certain skin lesions. Last year a dermatologist had sent to Dr. Blackburn a patient suffering from eczema; the patient had obvious myxœdema. The eczema had cleared up as a result of the administration of thyreoid extract. Another patient, seen some years ago, a nurse, had suffered from oft recurring urticaria. After taking thyreoid extract in quite small doses, up to 0·18 gramme (three grains) a day, she had lost her urticaria; she still took thyreoid extract and had said recently that she was never affected with urticaria. It was worth bearing in mind that a dry skin might be benefited by the administration of thyreoid extract.

Dr. Blackburn was pleased to note that Dr. Stokes did not agree with Thurmon and Thompson, who, in their alleged statement, remarked that hypothyreoidism was usually well marked or absent altogether. Obviously this was absurd. Patients in the early stages of myxœdema did not complain of the obvious symptoms of advanced myxœdema, but of various nervous manifestations *et cetera*.

Dr. Holmes à Court had mentioned the occurrence of symptoms of hyperthyreoidism and hypothyreoidism together. Dr. Blackburn had seen a patient suffering from such a condition in the Royal Prince Alfred Hospital. In this case there was a remarkable œdema of the legs; an impression made by the finger remained for a week. Apparently this had been a myxœdematous condition.

The relationship between hypothyreoidism and cardiovascular disease presented a very difficult problem. As Dr. Stokes had pointed out, most myxœdematous people were at a period of life at which cardiovascular disease was most common. Dr. Blackburn had seen younger myxœdematous people who had no signs of cardiovascular disease. He particularly remembered one patient who, after treatment, turned out to be a handsome young woman instead of a fat, unprepossessing female who looked old enough to be her husband's mother.

He agreed with Dr. Gillies that diet was of no importance. If the patients were not going to be given thyreoid extract, undoubtedly they should be given a diet that would prevent œdema; but, providing they were given thyreoid extract, they could eat what they liked.

In discussing the sensitiveness of myxœdematous people to thyreoid extract, Dr. Blackburn remarked that the severer the case, the smaller should be the dose to commence with. Patients suffering from the disease in a moderately severe form could take larger doses. He had recently been called in consultation to see a patient whose basal metabolic rate had been as low as −42%. On account of the severity of the condition, the patient's medical adviser had commenced treatment by giving large doses—0·3 gramme (five grains) a day. As a result the patient had become delirious, passing her motions under her and throwing herself about in the bed. The appearances had been suggestive of some cerebral condition; Babinski's sign had been positive on either side. The condition had cleared up rapidly when the administration of thyreoid extract was discontinued. The patient had progressed favourably when given small doses. In another case Dr. Blackburn had found it necessary to give as much thyreoid extract as 1·02 grammes (seventeen grains) a day; when the dose was reduced to 0·72 gramme (twelve grains), the condition had retrogressed. Dr. Blackburn found generally that between 0·3 gramme (five grains) and 0·42 gramme (seven and a half grains) was sufficient.

Dr. Stokes, in reply, expressed his thanks for the kind reception that his paper had received. He remarked that Dr. Gillies had hit the nail on the head when he had stressed the necessity for "spot" diagnosis. In regard to dosage, he mentioned that patients suffering from myxœdema were very sensitive to thyreoid medication, and stated that Byrom Bramwell had reported the case of a patient who had been able to tolerate minute doses only. The occurrence of cramps, Dr. Stokes thought, might be due to a vascular disturbance rather than parathyreoid deficiency. He agreed that persons suffering from myxœdema in its early stages were very frequently missed. Supraclavicular pads were not always evidence of hypothyreoidism. Dr. Stokes agreed with Dr. Walker in his view that the subject of myxœdema was worthy of discussion, although it was so well known; the fact that a remedy was available was all the more reason why everything possible should be known about the condition. Dr. Stokes thought that diet might be of importance. Dr. Steel had mentioned the value of iodine; Dr. Stokes believed that food should contain an adequate quantity of iodine. Foods rich in cholesterol should be restricted, not necessarily eliminated from the diet. In conclusion, he mentioned that *xanthoma tuberosum multiplex* was among the skin lesions sometimes associated with hypothyreoidism. He had recently attended a patient suffering from this condition; results of treatment by means of thyreoid extract had been satisfactory.

NOMINATIONS AND ELECTIONS.

THE undermentioned has been elected a member of the Victorian Branch of the British Medical Association:

Morris, Geoffrey Newman, M.B., B.S., 1932 (Univ. Melbourne), Infectious Diseases Hospital, Fairfield, N.20.

Obituary.

HAMPDEN CARR.

WE regret to announce the death of Dr. Hampden Carr, which occurred at American River, Kangaroo Island, South Australia, on September 30, 1932. The son of Colonel George Carr, of the Indian Army, he was born at New Ross County, Wexford, Ireland, on March 2, 1868. He graduated at Dublin, and at the age of twenty-three came to Australia and entered into private practice at Mount Lofty and later at Port Pirie, South Australia. At the age of twenty-seven he married Emmie Bevan Cooper, second daughter of the late Arthur Bevan Cooper, of Henley-on-Thames and of Adelaide. There were four sons and one daughter. The eldest son, Howard, was killed in action during the Great War.

In 1911 Hampden Carr moved to Unley, Adelaide, where he carried on an extensive practice, devoting much time to surgery. Needing lighter work, he left Adelaide for Kangaroo Island in 1924, where he practised until his death. He was loved by the people of Kangaroo Island, and he will be greatly missed, not only for his skill in practice, but also for his great understanding and kindliness.

ARCHIBALD WARDEN GRAVES MURRAY.

DR. ARCHIBALD WARDEN GRAVES MURRAY, who was killed in a motor car accident near Colac, Victoria, on September 23, 1932, was the son of Mr. and Mrs. C. T. W. Murray, of Manly, New South Wales. He was born at Sydney on June 16, 1888. He went to Brisbane Grammar School and subsequently studied medicine at the University of Sydney. He went into residence at Saint Andrew's College. He stroked the college boat and was noted as a first class swimmer. He was one of the original batch of medical graduates who qualified in 1915 and who went to England to join the Royal Army Medical Corps. Murray saw service with the Twenty-Ninth Division at Gallipoli. After the landing he was invalided to England *viâ* Mudros. He was sent to the General Hospital, Camberwell, London. Subsequently he joined the East Kent Regiment (The Buffs) in France. After being sent back to England again he was appointed Chief Medical Superintendent for East Anglia, with headquarters at Norwich.

After his return to Australia from the war, Murray gained some experience with Dr. Earle Page, at Grafton, and held resident appointments at the Newcastle Hospital, New South Wales, and at the Royal Hospital for Women, Paddington. He then practised for a while at Cairns, North Queensland, and on being appointed to the Ayr Hospital, practised in that town. Later he transferred his activities to Colac, Victoria, where he was practising at the time of his death.

Throughout his life Murray kept his interest and keenness in sport. While he was in England he won a swimming race for army officers against all-comers at Eastbourne. At Colac he was President of the Golf Club and was a member of the Tennis, Gun and Race Clubs. His sudden death has been a blow to a large circle of friends, and much sympathy has been shown to his parents.

SYBIL JEAN HAWKINS.

DR. SYBIL JEAN HAWKINS was born on April 27, 1901, at Clifton Hill, Melbourne. She was the youngest child of the late William J. Hawkins, leather merchant, of Fitzroy. She began her school life at the age of four and a half years at the Alfred Crescent State School. When she had completed a year in the sixth class she was *dux* of the school. She then attended the Fairfield Park State School and from there won a Government scholarship and half a scholarship given by the Presbyterian Ladies' College, where she studied for five years. In 1918 she was *dux* of the school and won the exhibition in physiology at the Melbourne University public examination. Prior to her entering the University she won a State exhibition. At the early age of eight years she decided to "be a doctor, as she could not think of anything better".

She entered the Melbourne University and began her medical course in 1919. At the end of the first year she won the Exhibition in Biology. In 1924 she graduated as Bachelor of Medicine and Bachelor of Surgery.

She was *locum tenens* in a Gippsland town and later, for a short time, served as resident officer at the Children's Hospital, Melbourne. She then started private practice at North Fitzroy, but in 1927 relinquished it to become a resident officer at the Queen Victoria Hospital. During the time she was there it was discovered she was suffering from pulmonary tuberculosis. At once she went to the country for a rest and open air life. At the end of three months, feeling improved in health, she received the appointment of Resident Medical Officer at the Wangaratta Hospital, but her health giving way again, she had to leave.

In April, 1928, she started practice in Warracknabeal, but after six months she was again forced to give up and returned to Melbourne at the end of that year.

In April, 1929, she was appointed Resident Medical Officer to the Janefield Sanatorium, which position she held until March, 1930, when she became ill and was for some weeks a patient there. From Janefield she was transferred to the Austin Hospital, where she remained until her death on September 30, 1932.

A fellow practitioner, who wishes to remain anonymous, writes:

The death of Sybil Jean Hawkins on September 30 last removed from the ranks of the medical profession one whose mind and intellect and zest for work had given rich promise of good results in the profession she had chosen.

The years between graduating at the University of Melbourne and her death she passed in alternating periods of illness and service as resident medical officer at various hospitals. The Queen Victoria Hospital for Women, the Wangaratta District Hospital, and the Janefield Sanatorium

all knew the excellent quality of her work, which, with her character and whimsical sense of humour, endeared her to all her colleagues.

Those few who knew her well during the last years of her illness are able to appreciate to the full the magnificent courage and never-failing cheerfulness with which she faced set-back after set-back in health, until she knew beyond all doubt what her inevitable fate must be.

Her sense of humour remained irrepressible by all the "bludgeonings of fate". Her courage and cheerfulness remained unconquerable to the day of her death and leave an imperishable memory and inspiration to those who were privileged to witness them.

Correspondence.

SHOCK AND ITS TREATMENT.

SIR: It was noticed, in perusing the report of the discussion that followed the reading of two papers at a meeting of the New South Wales Branch of the British Medical Association at the Assembly Hall on August 25, 1932 (Vol. II, No. 17, October 22, 1932), that Dr. D. Glissan, in speaking on "Shock and Its Treatment", was reported to have said "that he knew of no hospital in Sydney where provision was made for the treatment of shock cases".

It is deemed necessary, therefore, for the information of Dr. Glissan and that of practitioners generally, to point out, by means of this journal, that the Royal Alexandra Hospital for Children has had such a ward in constant operation for the past five years.

This is a six-bed ward attached to the surgical block, where "shocked" cases only are treated. The ward is maintained at an even temperature of 70° to 80° F., and special senior nursing exclusive to this ward is provided both day and night. All street accidents, head injuries, burns and "shocked" admissions of any kind are admitted directly to this ward from the casualty department or from the ambulance with no formality. A cot continuously warmed by means of hot water bottles and with the foot of the cot raised is in readiness at all times, and the ward is provided with special anti-shock and resuscitation equipment. The routine insures that a resident medical officer is automatically informed of the admission from the admission office and is at the bedside almost as soon as the child is placed therein, and all patients in this ward are kept on a quarter, half or hourly pulse chart.

In addition to these admissions, cases of post-operative shock and those that require more especial supervision owing to the possibility of hæmorrhage after operation, are nursed in the shock ward as long as is considered necessary. Hare-lips, cleft palates, intussusception cases, cases of pyloric stenosis, splenectomies, craniotomies, thyreoidectomies and the like are therefore transferred there immediately after operation.

It is to be understood that the shock ward at the Royal Alexandra Hospital for Children is regarded and maintained as a unit of the hospital, just as essential as the casualty department, the out-patients' department and the operating theatres.

Yours, etc.,

S. W. G. RATCLIFF,
Chief Executive Officer and
Medical Superintendent.

Royal Alexandra Hospital for Children,
Camperdown, New South Wales,
October 25, 1932.

THE FUTURE OF MEDICINE AS A PROFESSION.

SIR: Would you please allow me space to congratulate Dr. Kinsella on his recent able and courageous remarks on this subject? I am surprised that no one has already done so, for anyone who cares to consider our economic future must be filled with foreboding.

Before the war, when charity was charity, medicine was a comparatively well paid profession. In later years governments have vied with each other in providing social services, particularly free treatment of the sick, and our profession, though often enough receiving slight thanks for its services, has acquiesced. Occasionally we paused to wonder if all was well, but so long as the post-war money lasted, the phenomenon occurred of the profession waxing more and more prosperous while more and more people sought free treatment. In short, we recouped ourselves from our remaining private patients, but now, as Dr. Kinsella points out, many of the remaining ones are being forced by necessity to seek charity. Moreover, though it is well known that the ever-increasing complexity of medical science has raised the cost of medical attention enormously, it is not always realized that this same factor necessitates an ever-increasing number of doctors to care for a given number of people.

Thus on the one hand we have socialism, depression and increased medical costs rapidly thinning the ranks of those able or willing to pay. On the other hand, the advancement of medical science necessitates more doctors, the depression is increasing the number of students, and socialism, with free education for the many instead of the especially able few, has the same effect. Not all of these factors are necessarily constant, but, taking things as they are and are likely to be, we find that each leads to more and more doctors and fewer and fewer paying patients.

The logical conclusions stare us in the face. We can go on as at present, making temporary makeshifts, but we are doomed to a losing battle. No doubt, if we could present a united front, there would be something gallant in our fighting on, and the last of the private doctors might even rival the charge of the Light Brigade as a subject for heroic verse, but I fear that with our profession's genius for disunited action the retreat would be anything but gallant; we would, in fact, retire as a rabble, with the devil taking the hindmost, as he is already.

There is, of course, nothing for us but organization of some kind. We realize this in a dim way, and in many places we are already making rather twopenny-halfpenny efforts, but our actions are spasmodic, are opposed by vested interests and are on a scale insufficiently large to insure any lasting and real success. Meanwhile, in the background looms the fear that the State, that is, some vote-hungry politician, will suddenly enter the arena and do the organizing for us. The crux of the matter is whether we will do the organizing ourselves or wait till the State does it for us.

Although filled with admiration for the way in which the leaders of our association endeavour to increase our scientific knowledge, one is forced to wonder what they are about in the economic field. One knows that they spend long and thankless hours adjusting many matters of more or less importance, but has not this preoccupation with detail tended perhaps to obscure the view? Maybe our lack of vision is one of the defects inherent in our specialized education and way of life.

If ever our profession needed wise leadership it is now. By constant endeavour our forbears raised our status from that of menials to one of the most honoured in the land, and it behoves us, not only for our own advantage, to maintain what they have striven for. The medical profession has no wigs or robes or great offices of State to enhance its dignity in the public eye. Whatever honour it obtains is by its daily dealings with the great mass of the people. Has it the same honour, the same place in the affections of the people as it had, say, twenty years ago? Human nature being what it is, how long do we suppose our honour will last when the struggle for shillings becomes really intense? Will our honorary service—already taken for granted and presumed on to the uttermost—our devotion to medical science, our willing sacrifice at times of health and life, the sterling integrity of our elect compensate in the public mind for the general scramble?

This concern about our honour is not idle, for it is the foundation of the whole structure of medical practice. For the few honour may be compatible with poverty, but most of us are only mortal and have mortals dependent

on us. Once let the public become really aware of the "menace of the hungry doctor" and it will be a matter of moments only till the State steps in. And rightly so.

Here, then, is our need for leadership. Within our ranks are men with fine intellects and high characters. Not always have these sought office, but if they now will come to the fore, I for one am satisfied that we have sufficient genius to erect whatever organization may be necessary, to adapt our economics to the altered social structure, to free ourselves from the taint of commercialism, to banish the despair demoralizing our younger men, and to augment the usefulness of what we all in our innermost hearts believe to be the finest calling on this earth.

In conclusion I may say that there is not an original thought in the whole of this letter, which is merely an attempt to make articulate thoughts that are in many minds. It is pathetic to watch our profession, so potentially powerful, behaving like a bemused giant.

Yours, etc.,

"ONE OF THE TOO MANY."

November 3, 1932.

THE PRICE OF ETHER.

SIR: I have long hesitated to introduce anything savouring of politics into our journal, but I think the matter of the price of ether should be investigated.

For years ether has been produced in this country at a reasonable figure, but on the introduction of the prohibitive tariff of last year the price advanced by over 50%. This was despite a considerable fall in the basic wage and follows the formation of a combine. May I also point out that the raw material, ethyl alcohol, is worth under a shilling a gallon, and on being subjected to a very simple chemical process the price becomes over £2 per gallon.

It is true, this is but a small cost in the upkeep of a practice, but still a principle is involved.

Similarly "Kelene" costs but 3s. 6d. per 100 cubic centimetres in England and 14s. 6d. made in Australia.

Yours, etc.,

"FAIRPLAY".

October 16, 1932.

Books Received.

ONE HUNDRED POPULAR FALLACIES, by C. W. Budden, M.A., M.D., Ch.B., 1932. London: John Bale, Sons and Danielsson, Limited. Crown 8vo., pp. 170. Price: 3s. 6d. net.

ARTIFICIAL PNEUMOTHORAX (PRACTITIONERS' SERIES), by L. S. T. Burrell, M.A., M.D., F.R.C.P.; 1932. London: William Heinemann (Medical Books) Limited. Demy 8vo., pp. 181, with illustrations. Price: 12s. 6d. net.

MATERIA MEDICA OF PHARMACEUTICAL COMBINATIONS AND SPECIALITIES, by U. B. Narayanrao, with introduction by G. V. Deshmukh, M.D., F.R.C.S.; 1932. Bombay: Rayan Pharmacy. Crown 8vo., pp. 292. Price: 6s. net.

Medical Appointments Vacant, etc.

FOR announcements of medical appointments vacant, assistants, *locum tenentes* sought, etc., see "Advertiser," page xvi.

GOVERNMENT OF TONGA: Medical Officer.

LAUNCESTON PUBLIC HOSPITAL, LAUNCESTON, TASMANIA: Resident Medical Officer (male).

ROYAL HOSPITAL FOR WOMEN, SYDNEY, NEW SOUTH WALES: Resident Medical Officer, Junior Resident Medical Officer.

SYDNEY HOSPITAL, SYDNEY, NEW SOUTH WALES: Honorary Officers.

THE UNIVERSITY OF MELBOURNE, VICTORIA: Lecturer in Medical Ethics.

Medical Appointments: Important Notice.

MEDICAL practitioners are requested not to apply for any appointment referred to in the following table, without having first communicated with the Honorary Secretary of the Branch named in the first column, or with the Medical Secretary of the British Medical Association, Tavistock Square, London, W.C.1.

BRANCH.	APPOINTMENTS.
NEW SOUTH WALES: Honorary Secretary, 135, Macquarie Street, Sydney.	Australian Natives' Association. Ashfield and District United Friendly Societies' Dispensary. Balmain United Friendly Societies' Dispensary. Friendly Society Lodges at Casino. Leichhardt and Petersham United Friendly Societies' Dispensary. Manchester Unity Medical and Dispensing Institute, Oxford Street, Sydney. North Sydney Friendly Societies' Dispensary Limited. People's Prudential Assurance Company Limited. Phœnix Mutual Provident Society.
VICTORIA: Honorary Secretary, Medical Society Hall, East Melbourne.	All Institutes or Medical Dispensaries. Australian Prudential Association, Proprietary, Limited. Mutual National Provident Club. National Provident Association. Hospital or other appointments outside Victoria.
QUEENSLAND: Honorary Secretary, B.M.A. Building, Adelaide Street, Brisbane.	Brisbane Associated Friendly Societies' Medical Institute. Mount Isa Mines. Toowoomba Associated Friendly Societies' Medical Institute. Chilliagoe Hospital. Members accepting LODGE appointments and those desiring to accept appointments to any COUNTRY HOSPITAL are advised, in their own interests, to submit a copy of their agreement to the Council before signing.
SOUTH AUSTRALIAN: Secretary, 207, North Terrace, Adelaide.	All Lodge Appointments in South Australia. All Contract Practice Appointments in South Australia.
WESTERN AUSTRALIAN: Honorary Secretary, 65, Saint George's Terrace, Perth.	All Contract Practice Appointments in Western Australia.
NEW ZEALAND (Wellington Division): Honorary Secretary, Wellington.	Friendly Society Lodges, Wellington, New Zealand.

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